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Brain

A Journal of Neurology

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BRAIN.

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THE UPWARD MOVEMENT OF THE EYES.¹

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New points of view evolve with the growth of knowledge. Thus there has been a natural tendency of recent years, which becomes increasingly more apparent as information regarding normal and pathological structure accumulates, to regard neurological problems in relation to conceptions of function rather than from the strictly anatomical standpoint. The genius of two former presidents of this Society—Dr. Hughlings Jackson and Sir Charles Sherrington—has been largely responsible for the attainment of this outlook. In like manner our attention will no doubt be focused more and more upon the genesis of disease rather than upon its results, as represented by the pathological changes in the tissues.

The clinician is continually engaged from his earliest days in acquiring a practical knowledge of disease. Most of us pass through a stage during which the rarities and the unusual attract our attention and appeal to our enthusiasm, while at a later period a closer study of the commoner disorders and phenomena, with particular reference to the application of general principles, engenders a fresh interest. With increasing experience one's outlook widens, one learns to look at things from different points of view, and one is more and more conscious of personal limitations, and impressed by the limitations of knowledge and by the great field for clinical observation which lies before us.

I have selected as the theme for these remarks "the upward movement of the eyes." My purpose is to indicate some of the many questions which arise when we regard an apparently simple phenomenon

¹ Presidential Address delivered to the Neurological Section of the Royal Society of Medicine upon October 18, 1927.

from a variety of standpoints. The title I have chosen is perhaps misleading, for it is not my intention to attempt an exhaustive disquisition. Again the choice of subject may appear to be presumptuous, for I do not flatter myself that anything I have to say is new to you.

Some weeks ago, just as the light was failing, I was struck by the behaviour of an owl perched upon an isolated branch. The small birds around him were twittering in alarm, and from time to time the owl turned his head suddenly, first to one side then to the other. The observation was new to me, although probably familiar to some of you, for my children tell me that they have often watched an old owl in the Zoological Gardens and noticed these sudden movements of the head. A simple observation may serve to arouse a train of thought. Presumably the movements of the owl were determined by the sounds in his vicinity, and presumably he turned his head in order to visualize the better his surroundings. Why is it that in man we never see these sudden movements of the head, for the eyes of man like those of the owl are set far forward and the owl's vision, as is the case in man, must be binocular? I recalled the observations of Wilfred Harris [1] who noted that birds have little if any power of movement of the eyes, and that in the birds, including the owl, there is a complete decussation of the visual fibres at the chiasma. The owl is obliged to move his head since he cannot otherwise fix his eyes upon his prey. Such sudden movements of the kind must make his presence more evident, yet this is not perhaps a matter of material moment since the owl is a bird of the night and in this respect peculiar.

The co-ordinated movements of the head and eyes in man are obviously regulated by a mechanism of extreme beauty and delicacy. We are constantly moving the head and eyes for purposes of vision, the object to which our attention is directed providing the stimulus which determines the movement called for. The visual movement mechanism in man is determined by the demands of stereoscopic vision, and the importance of these co-ordinated movements is apparent when we recall that they constitute a precursor to the acquisition of specialized purposive acts, even though such acts may subsequently become more or less automatic by repetition.

Then, too, it is interesting to note that the relative degree to which we bring into play the movements of the head and of the eyes respectively in relation to visual fixation must be fairly constant under normal conditions, for, although both sets of movements can be utilized independently for visual purposes, pronounced rotation of the head to



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one side without an associated deviation of the eyes, or pronounced deviation of the eyes to one side, the head remaining fixed, are movements so unusual that they at once arrest attention. The actor is well aware of this and he exaggerates those independent movements of the head and eyes to which a conventional meaning has come to be attached for purposes of emphasizing his emotional expressions.

Further, the co-ordinated movements of the head and eyes afford a very beautiful illustration of the dictum, which we associate with the name of Dr. Hughlings Jackson, that movements not muscles are represented in the cortex. Indeed the contraction of the homolateral sternomastoid in association with deviation of the eyes to the opposite side, as seen both on voluntary movement and in the cortical fit, is perhaps the most striking instance of the preponderating participation of a homolateral muscle in a co-ordinated movement.

The acquisition of co-ordination is a subject of entrancing interest, raising as it does questions of functional adaptation. Is it not a remarkable fact that the new-born chick should walk about and pick up its food as soon as it emerges from the egg, whereas the young nestling is at first so helpless? Co-ordinated movements are for the most part acquired and not innate and, speaking generally, the more specialized a co-ordinated movement the later its development. This certainly applies to the more highly specialized movements of man.

All of us have watched with interest the inco-ordinate movements of the young infant. The eyeballs are seen to roll in various directions, and they tend to move to some extent independently of one another with the result that the child often squints. Preyer [2], who has made this ~~part~~ the subject of special study, writes: "Some new-born children actually make associated, co-ordinated movements of the eyes several times on the first day: others do not, but I never found in any child co-ordinated movements exclusively . . . on the whole, I have found that, in the newly-born, one eye very often moves independently of the other, and the turnings of the head take place in a direction opposite to that in which the eyes move. The unintentional character of both movements is plainly recognizable, and the combination of the two is, at the beginning of life, accidental. The turning of both eyes to left and right, also, which is established on the first day, takes on the appearance of accident, coming in as one among all possible movements. The co-ordinated movement of the eyes determines the ability to fixate, and fixation of the eyes is a voluntary movement determined by the will. Gradually the inco-ordinate movements become less noticeable

until, by the end of the third month or thereabouts, they are no longer observed. The innervation of the eye muscle offers, as Sir George Berry [3] truly remarks, "one of the most beautiful and most easily studied examples of the development of a habit." But it is further of interest to note that whereas, according to Preyer, the ability to follow a moving object with the eyes is not usually noticeable before the close of the third month, the ability to turn the head towards a bright light, so that this can produce an image on the retina, is often present on the day of birth. We see here an illustration of the principle that more specialized movements are acquired at a later date than those which are less specialized?

It is a remarkable fact that once the habit of co-ordination of the eye movements has developed in response to visual fixation, the eye muscles cannot be individually activated. Most of us can probably cite exceptional cases in which an individual was able to contract an isolated muscle apart from a co-ordinated movement in which it regularly takes part, but I know of no instance in which, the ocular muscles being intact, it was possible voluntarily to move one eye independently of the other. The call for co-ordination in relation to vision would seem to be so powerful, and the cortical representation of the co-ordinated movements consequently so indelibly fixed as such, that this is an impossibility. It would indeed appear that, if a habit movement is developed in relation to an essential function, no isolated contraction of a muscle concerned can be brought about should this in any way interfere with the specific function in question: in other words, one is perhaps justified in saying that complexes of action are fixed in the cerebral cortex in relation to the necessity for their performance.

The great majority of people do not follow a special occupation or pursuit which necessitates the frequent fixation of the eyes upon an object above the level of the head. Indeed, one may say that the objects which engage our attention are almost always situated at or below the level of the eyes. When walking we may watch our feet in order to avoid obstacles or glance from side to side to avoid the traffic, but we seldom look upwards for we have no fear of something falling on us or of an attack from above. We rarely look up, we are indeed, not in the habit of doing so, for we do not anticipate the unexpected. An illustration in point is afforded by the children's game of "hunt the thimble," for I can tell on good authority that when the object which the children are looking for is placed just above the line of vision, even though in a conspicuous place, it often

escapes detection. So unaccustomed are we to look up for any length of time that when we spend a long morning in a picture gallery we are reminded of our exceptional experience by the aching of the muscles of the neck or by headache. When we look upwards the eyes are commonly "directed into space," and assume a position of parallelism. I take it that the type of headache to which I have just referred is a consequence of "eye strain" determined by the effort called for in producing the degree of sustained convergence, an unaccustomed movement with the eyes in this position, which is required in fixing objects in our near vicinity situated above the level of the line of vision.

But while, when we look upwards, our gaze is almost always so directed for the express purpose of visual fixation, we may look upwards for other reasons. Some of you are probably familiar with the remark addressed by the schoolmaster to the pupil, "You won't find the answer in the ceiling." While the child's action is capable of other possible explanations, you will, I think, agree that some of us look upwards in periods of mental abstraction, presumably in order to give our association of ideas free play by eliminating visual stimuli which might interrupt or interfere with our train of thought. The same result might be as effectively achieved by closure of the eyes, but this is exceptional, possibly because the movement is too obvious, or for other reasons. The possibilities occur to me that the movement of looking upwards in association with mental abstraction may in some instances be determined by a primitive convention, in other words, by the hope of inspiration from above, or that it may be of the nature of a release phenomenon. Both these suggestions appear to me, however, unlikely. My impression is that the movement is voluntary and purposeful; this is certainly so in my own case, although it may become a habit.

The changes in expression associated with mental abstraction on the one hand, and mental concentration on the other, are striking. Among other distinctive features the pupil tends to dilate in states of mental abstraction and to contract during mental concentration. I often recall the words of one of my teachers, Professor John Wyllie, who when examining the eyes with the ophthalmoscope would say to the patient in a "musical, dreamy hypnotic tone of voice, "Think of your distant home." There is a children's game which provides another illustration. The child says to his companion, "I can read your thoughts by looking into your eyes." He asks his playmate to think of a number, let us say the number 1, and then to think of another number, say 100. After asking him to repeat this several times he

says to him, "Now think of either one or a hundred and I will tell you the number you are thinking of." In nine cases out of ten he is right, for when one thinks of the larger number one's pupils tend to dilate, while, when one thinks of the smaller number they contract. This, however, is by the way. Again, the upward movement, or the direction upwards of the eyes, is a stereotyped characteristic of the suppliant or devotional attitude, as the works of the old masters constantly remind us. The domicile of the Deity is by common consent located in the heavens above, an obvious reason why the eyes should be directed upwards in addressing or approaching the Almighty.

Further, the movement of turning up of the eyes has come to be utilized as a conventional mode of expression. Thus certain individuals are in the habit of turning up their eyes, either in association with or independent of spoken language, in order to express or accentuate their meaning. Thus I overheard a young girl remark to her companions: "Oh, if I had heard her say that I should have turned up my eyes!" What did she mean? My impression is, that she intended thereby to imply disapproval or doubt, for these appeared to me to be the conventional meanings which are attached to and implied by this movement. But I may remind you that, as Darwin [4] points out, different races attach different meanings to the same expressive movement just as they employ different languages with which to express their thoughts. A conventional expressive movement must have an origin. It may be that the upward movement of the eyes, when employed to express disapproval, had its primitive origin in a desire on the part of the individual to avoid seeing that which met with his disapproval, or it was perchance an appeal to the Almighty to help him to resist temptation.

Individuals vary greatly in the extent to which they exhibit or employ facial movements in relation to expression. At the one extreme we find the country yokel with a face so immobile as to suggest the Parkinsonian mask, while the actor, on the other hand, employs expressional movements in an exaggerated form. The similarity between the physiognomy of an illiterate ploughman with an almost complete absence of expressional response, as compared with that of a patient who exhibited a slight degree of encephalitic Parkinsonism, recently afforded me an interesting subject for discussion. In the one case the individual had not acquired the habit of using his muscles of expression, whereas, in the other, the movements of expression were interfered with as a consequence of an organic lesion of the nervous

system. Cerebral activity, beyond doubt, plays an important rôle in the acquisition of expressional movements. One recalls Millet's famous pictures of illiterate peasants working in the fields, carrying out their daily duties with machine-like regularity, with empty minds, and with little opportunity for that intercommunication between man and man which plays such a prominent part in creating and stimulating the thinking brain.

But I would remind you that we are trained from early childhood to control emotional display, and that great differences are met with not only in individuals but also in different races. I recall the words of one of our most famous tragedians to the effect that the great actor passes through three phases—firstly he, so to speak, learns his part; secondly, he comes to feel and live the part; and finally he arrives at a higher sphere when he utilizes all the necessary emotional expressions with telling effect, although these are divorced from any corresponding emotional feeling.

Mimicry and mannerisms.—Expressional movements are used by all of us in varying degree. They constitute up to a point a means of intercommunication, especially in relation to the emotions, and are thus comparable with language. Darwin's references [5] to the case of Laura Bridgman certainly suggest the possibility that in some instances such movements may be innate, but all the probabilities would seem to indicate that they are usually acquired. Custom has attached conventional meanings to certain movements, and these are picked up just as is language—although the child receives no special training unless it be that he is commonly corrected should any tendency to exaggeration be noticed. Whatever be the primary origin of a conventional movement there can, I think, be no question that unconscious mimicry is commonly responsible for its transmission. Some individuals are, however, much more prone to acquire such movements than are others. Striking similarities in expressional behaviour are often noticeable in members of a family and in the case of individuals who are brought much in contact with one another. If one watches a number of persons sitting round a room, listening to speakers who are in turn expressing their views upon a subject in which those present happen to be especially interested, or regarding which they hold strong opinions, one notices on the part of some of the listeners a tendency to adopt a pose very similar to that adopted by the speaker, whereas others, on the contrary, adopt an indifferent or antagonistic attitude. The sympathetic listener would appear to unconsciously assume the posture of the speaker either

in order that he may the better appreciate the mental attitude of the latter, or for the purpose of indicating to the speaker and those present his agreement with the views expressed, or it may be to emphasize to himself or those present his open-mindedness, i.e., his preparedness to give the speaker an impartial hearing—although he may not be prepared to express a positive acquiescence.

When a movement of the kind which is unusual or exaggerated becomes habitual, we term it a *mannerism*. All of you have no doubt been struck by the way in which assistants are apt to acquire the mannerisms of their chiefs. I well remember attending, as a student, a clinical lecture delivered by a distinguished surgeon who had a habit of puffing out his cheeks. His assistant surgeon and clinical tutor stood behind him with folded arms listening to his words, and both were quite unconsciously indulging in the same grimace. This incident provides an illustration of the development of a mannerism by mimicry, the way in which many of the expressional mannerisms are certainly acquired. There are, however, other ways, and the habit of "turning up of the eyes" usually originates, I think, as a purposive act. One may turn up the eyes in order to emphasize one's disapproval, and again, one may acquire the habit of doing so, unconsciously, when one would not express disapproval or doubt in words, either because one does not wish to wound the susceptibilities of the individual, or it may be for other reasons.

When an habitual movement at first purposeful becomes purposeless, it falls into the group of the *tics*. A mannerism becomes a tic when it is dissociated from the conditions or the purpose which originally gave rise to it. We sometimes meet with cases of upward movement of the eyes in which the movement, at first a mannerism, becomes a tic. A case recently met with is of interest in this connection, for it indicates, not only the development of the upward movement of the eyes as a tic, but also raises an unusual point in diagnosis. The patient, a girl, aged 14, had had two major epileptic seizures. Her mother stated that on each occasion the fit had been preceded by turning up of the eyes, but she added that this movement did not strike her as unusual since, she said, the girl often turned up her eyes, especially when preparing her lessons. I suspected that the patient was subject to attacks of *petit mal*, but when I questioned the girl—and I had no reason to doubt her statement—she remarked in words to this effect, "Oh, that's nothing; it is just a habit I have got into. You see, the girls in my class don't always approve of what our school teacher says, and when we disapprove

we just turn up our eyes. There are several girls in the class who do the same thing, and I have just got into the habit of doing it."

The upward movement of the eyes, though not uncommon as a mannerism, is, in my experience, uncommon as a tic, possibly because the movement is so apparent that its occurrence attracts attention, and is thus less likely to be unconsciously imitated.

The eyes commonly deviate to one side during a generalized or unilateral epileptic fit. I cannot say whether they are ever directed upwards or downwards, but I have had no recent opportunity of making observations on the point. It is indeed surprising that a phenomenon may have constantly occurred before one and yet have escaped notice, unless one's attention has been for some special reason directed to it. On the other hand, the relatives and friends of an epileptic patient not unfrequently state that the eyes move upwards in slight attacks, and I have myself seen two patients recently, during attacks of *petit mal*, in which the eyes turned almost directly upwards. More commonly, however, the patient merely stares. I know of no series of observations upon the position of the eyes in epileptic attacks, but I have the impression that the analysis of a collected material directly bearing on this point might prove informative in relation to the seat of origin of the attack, and possibly helpful in prognosis and treatment. The subject is one which, it seems to me, is well worthy of the attention of those who have special facilities for observing patients during attacks.

The cortical representation of the upward movement of the eyes.—The upward, downward and convergent movements of the eyes can all be carried out voluntarily, and must consequently be represented in the cerebral cortex. I know of no reported case, however, in which a fit characterized by upward, downward or convergent movements of the eyes—or a paralysis of these movements—was associated with organic disease of the cerebral hemispheres. Again, those observers who have especially studied the effects of stimulation of the cortex in normal animals and in man have, so far as I know, failed to produce an upward or downward movement of the eyes. Hughlings Jackson [6] advanced an explanation to account for the facts which remains unchallenged. I may remind you that it occurred to Jackson that the lateral movements of the eyes might be so much more powerfully represented in the cortex, than any of the other ocular movements, that they overpower the latter when the eye-area is stimulated. Risien Russell [7], whose experiments were carried out at Jackson's suggestion, stimulated the "eye area" of the cerebral cortex on one side after

previously dividing the internal rectus of the eye on the same side and the external rectus of the eye on the opposite side and found he was then able to elicit upward and downward movements of the eyeballs. He consequently concluded that "Hughlings Jackson's suggestion as to the probable explanation why under ordinary circumstances none but the lateral movements of the eyes to the opposite side can be elicited on excitation of the one cerebral hemisphere, appears to be the correct one. . . . The other ocular movements are as truly represented in the cortex as is the lateral movement of the globes to the opposite side; the only difference is a question of degree in their representation, the latter being more powerfully, or more widely, represented than any other ocular movement."

An innate co-ordinated upward movement of the eyes.—My remarks hitherto have been confined to the upward movements of the eyes in so far as they appear to be more or less obviously referable to the cortex of the brain. There are, however, upward movements of the eyeballs, which seem to be more or less directly associated with, or related to, a "centre" situated at a lower level.

According to Preyer, the eyes of the new-born infant do not manifest any apparent co-ordinated movement which cannot be attributed to accident. I have, however, repeatedly noticed a tendency, when an infant was sitting half asleep on its nurse's knee taking a bottle, for the eyeballs to roll upwards exposing the sclerotic, in association with drooping of the lids, just as is the case in the adult who has difficulty in keeping awake. My impression is that this is a definite co-ordinated movement which is present at birth, and Mr. W. P. Kennedy, who has at my suggestion made some observations upon the eyes of infants during the first few days of life, came to the same conclusion. Assuming this observation to be correct, we have here an instance of a co-ordinated movement of the eyes which is no doubt of a lower order and which, unlike the co-ordinated movements determined by vision, is innate. In other words, while the co-ordinated movements of the eyeballs are essential to vision, the co-ordinated upward movement is exceptional in that it is present at birth, and presumably determined by a different type of physiological demand.

An upward movement of the eyes, of which the individual is unaware, occurs under normal conditions when the eyes are firmly closed. Although the phenomenon may not be easy to demonstrate in the healthy person, since it only occurs in forcible contractions of the ocular sphincter, it is very evident in cases of peripheral facial paralysis

or paresis in which the patient cannot close the eye, or in which the upper lid can be passively raised without difficulty. The rolling upwards of the eyes under such circumstances is of some clinical significance in the detection of slight degrees of facial paresis for, as the movement only occurs in association with powerful contractions of the sphincter, its occurrence indicates that the patient is making a real effort to contract the sphincter of the lids, and *vice versa*. This movement whereby the cornea is brought under the cover of the bony ridge of the eyebrow constitutes, with the associated closure of the eyes and contraction of the pupils, a very beautiful illustration of a protective mechanism.

Blinking.—The act of ordinary blinking or winking is accompanied by a synchronous upward rotation of the eyeball. Thus, according to Ponder and Kennedy [8], "Each blinking movement is associated with a movement of the eyes itself, the point of fixation being moved some 15 degrees, and the eye rapidly jerking upwards and inwards." These observers are of opinion that "the movements (of blinking) are centrally controlled and dependent on intermittent impulses passing from the region of the basal ganglia," and that "the act of blinking is closely related to the 'mental tension' of the subject at the time, the movements constituting in all probability a kind of relief mechanism, whereby nervous energy, otherwise unutilized, passes into a highly facilitated path." In support of this conclusion they remark that "states of abstraction," or more accurately absolute blankness of mind, "and states of intense but internally directed mental activity, such as when a mathematical problem is being solved, are associated with a slow blinking rate." While, on the other hand, "a state of mental tension which has no internal or external outlet, as impotent rage, anxiety necessarily accompanied by inactivity, or excitement which cannot be shown and expressed by physical movements, is accompanied by a rapid blinking rate." What then is the economic purpose of the elevation of the eyeball associated with the act of blinking? The eyelids brush the conjunctival surface like the windscreen wiper of a motor car, and it would seem that the purpose of the associated upward movement of the eyeballs is to aid in the sweeping of the conjunctiva and the disposal of the tears. In this connection it is interesting to note that young infants do not wink. This was my impression from watching my own children during early infancy, but I confess that the significance of the observation had not previously attracted my attention although it may be familiar to some of you. I was consequently much interested to find

that Ponder and Kennedy [9] observed that "True blinks first make their appearance about the age of six months, and even then are infrequent." This observation was, I understand, based on a single case and, if so, cannot be accepted as necessarily applying to all. It is interesting in this connection to compare the time when the infant first sheds tears. According to Preyer [10], two cases were observed by Darwin in which the eyes were wet with tears for the first time at the end of the third and ninth weeks, while in another case tears flowed down the cheeks at the end of the sixth week. Then again, one of Darwin's children first shed tears in crying in the twentieth week, while Champney's child shed tears for the first time in her fourteenth week. These facts would seem to suggest a time developmental relationship between the act of blinking and the shedding of tears. The question appears to me to be of interest in relation to emotional expression. I must, however, leave it at this point.

The position of the eyes during sleep.—The eyes roll upwards during sleep. We can all no doubt recall occasions when we have watched a companion whose eyes, to use a popular expression, were "heavy with sleep." We have seen his eyelids slowly droop, the eyeballs move upwards so that the sclerotic only is visible, the nodding movements of the head and the sudden start as the muscles generally relax, a series of phenomena which continues to recur despite all the efforts of the individual to keep awake. The upward turning of the eyes during sleep is not always easy to demonstrate, for on attempting to raise the upper eyelid of a sleeping person, unless he happens to be in a deep sleep, one may meet with a certain degree of resistance. This may perhaps be explained by a persistence of tone in the sphincter. My impression is, however, that there is an actual reflex contraction of the muscle which probably forms part of the reflex defence mechanism of sleep. Dr. W. R. Russell, my house-physician, who examined ten sleeping patients, found that in all there was some slight resistance on attempting to elevate the upper lid, that in all the pupils were contracted, that in six the eyes were directed straight forwards, in two slightly upwards and in two markedly upwards, although in one of these they almost immediately came down. These observations suggest that the contraction of the pupil occurs in lighter degrees of sleep than does the upward movement of the eyes, and that the sphincter tone or reflex persists, in some cases at all events, even when the pupils are contracted and the eyes turned upwards. Very exceptionally individuals sleep with their eyes open. The phenomenon is certainly very unusual for

Dr. Russell, who recently made inquiries throughout the hospital, was unable to find at the time a single instance. My two ward sisters tell me that, to the best of their recollection, the eyes are always turned upwards under such circumstances. According to Gowers [11], the eye remains partly open in cases of complete peripheral facial paralysis during sleep. I have, however, a case of complete peripheral facial palsy at present under my care, the only case of the kind I have had an opportunity of observing since my attention was directed to the point, in which the eye is completely closed during sleep although the patient cannot voluntarily close it when he is awake.

One sometimes hears the expression "the cadaveric position of the eyes," and I have heard it stated that the eyes turn upwards after death. While the eyes may turn up during the act of dying, there can be no doubt that after death the axes of the eyeballs are almost always if not invariably, in the normal position of rest, i.e., in the horizontal plane.

The position of the eyes during surgical anæsthesia.—A possible comparison between the position of the eyeballs in sleep and in surgical anæsthesia naturally suggests itself. Very little attention appears to have been paid to the eye movements in anæsthesia, probably because, as Dr. John H. Gibbs writes me, "These ocular movements are of very little practical use to the anæsthetist." The three anæsthetists with whom I have discussed the question are all in agreement that in the great majority of cases the globes remain central. According to Dr. Gibbs, "One meets with lateral deviation, but it is much less common than upward, whilst downward movement is, in my experience, very rare." Again he remarks, "With ethyl chloride, and with no other anæsthetic agent, I have repeatedly seen vertical nystagmus which passes off with deeper anæsthesia." Dr. J. S. Ross writes me, "During surgical anæsthesia the eyelids are usually almost closed with the eyeballs at rest and looking forward and slightly downwards. An extreme rotation downwards may usually be taken as a sign of a very deep anæsthesia." Dr. Torrance Thomson tells me that his impression is that a downward deviation of the eyes occurs more commonly than upward or lateral movements. Thus it would appear that deviation of the eyes is exceptional under anæsthesia, and that the behaviour of the eyes differs not only according to the depth of anæsthesia but also according to the anæsthetic which is used.

No series of observations has been published, so far as I am aware, upon the position of the eyeballs in man during anæsthesia. Further,

it is difficult to distinguish between voluntary and reflex movements. Risien Russell [7] has, however, I may remind you, recorded his observations upon the position of the eyes in dogs anaesthetized with chloroform and ether. He makes no reference to upward or downward movements of the eyes, although he noted a lateral deviation with great regularity, in most of the dogs to the right in a few to the left, about the time when surgical anaesthesia was about to be established. Dr. Hughlings Jackson's comments [6] upon these observations are of much interest.

The representation of the upward movement of the eyes in the brain-stem.—An isolated loss of the associated upward movement of the eyes is practically pathognomonic of a lesion within the substance of the brain-stem. There are, as is well known, many recorded observations in support of this conclusion. Evidence is afforded both by cases in which loss of the upward movement was met in association with a demonstrable post-mortem lesion, commonly a tumour, and by cases in which the accompanying symptoms, in the absence of post-mortem evidence, were clearly indicative of a lesion in this situation. Conversely, there is, so far as I am aware, no evidence that a lesion in any other part of the nervous system, the brain-stem being intact, ever results in an isolated loss of the associated upward movement of the eyes. Spiller [12] analysed the available facts in 1905. The lesion, in those cases which have been pathologically confirmed, was "in the vicinity of the oculomotor nucleus" and involved the adjacent region about the aqueduct of Sylvius. Although the clinical evidence points to an area in the brain-stem destruction of which results in loss of upward movement of the eyes, we possess, so far as I am aware, no more precise knowledge of the structural mechanism to which this specific disturbance can be definitely relegated. Lethargic encephalitis is in my experience much the most common cause of isolated paralysis of the upward movement.

Spurious paralysis of the upward movement of the eyes.—But while paralysis of the upward movement of the eyes is a distinctive focal sign, I have met with several individuals who had difficulty in raising, or indeed were quite unable to raise, the eyes above the horizontal when asked to do so, although they were able to elevate the eyes to the full extent if asked to follow the finger upwards. The apparent loss of power cannot be explained by inattention, or perhaps I should say by inattention only, since it was confined to the upward movement. Fixation of the eyes above the horizontal with the head erect is an

unaccustomed movement, and the infrequency with which we are called upon to direct our eyes upwards may account for this observation. The disability manifested by these patients would seem to be comparable with the known difficulty of converging without having an object on which to fix the eyes. Again, we find an analogy in the difficulty some individuals have in wrinkling the forehead, and even in expanding the thorax when asked to do so. Duane [13] writes as follows with reference to loss of the upward movement: "It is probable that some of the cases reported are spurious, the power of movement being present but never put forth. This was so in one of my cases, in which repeated examinations extending over several years always showed complete inability of the eyes to go upwards above the horizontal plane, and yet Graefe's test proved that they could really turn up at least 30° , and subsequently the patient regained the power of spontaneous movement."

Obviously it is important from the point of view of diagnosis to distinguish a spurious paralysis in which the patient does not move his eyes upwards when asked to do so, although there is no actual loss of power, from an actual paralysis of the upward movement of the eyes. Accompanying signs such as other extra- or intra-ocular palsies, absence of blinking, or the presence of vertical nystagmus on looking upwards, would point to a true paralysis. If a paralysis of the upward movement ever results from a lesion situated above the level of the brain-stem "centre" one might conceivably expect to find in such a case that the eyes rolled upwards when the eyelids were tightly closed. I have never, however, met with an instance of the kind although I have on several occasions examined cases of paralysis of the upward movement with this possibility in view.

Turning up of the eyes in encephalitic Parkinsonism.—Involuntary turning up of the eyes occurs in some cases of epidemic encephalitis. This symptom has attracted considerable attention during the past two or three years. There would appear to be no reference to it in the literature prior to 1923. According to Wimmer [14] movements of the kind were observed by Bing in only three in a total of about three hundred encephalitic patients, while Wimmer met with five instances in a somewhat similar material. I have notes of eleven cases in which such movements of the eye were remarked on. These figures, no doubt, underestimate the relative prevalence of the phenomenon since the movements in their slighter degrees cause little or no inconvenience. There were associated manifestations of Parkinsonism in all my cases and this would appear to be the universal experience. The symptom is

pathognomonic and is sometimes of diagnostic importance, since the accompanying indications of Parkinsonism may be so slight that the true nature of the malady might otherwise pass unrecognized unless by an experienced observer.

Two of my patients complained of "turning up of the eyes" as the only symptom causing disability or inconvenience. Among my eleven cases the eyes moved more or less directly upwards in eight; in one case the eyes were directed upwards at one period and downwards at another; in one they were sometimes directed upwards and sometimes downwards, while in another the movements were to the right and slightly upwards. No paralysis of upward movement was observed at the time of examination in the three cases in which downward and lateral movements occurred.

The deviation of the eyes may be momentary. On the other hand the eyes may be directed upwards for hours at a time although it may be possible for the patient to bring them down and keep them down for short periods by exercising "an awful effort," to use the expression employed by one of my patients. One patient stated that the eyes tended to turn upwards when he was in the house, whereas when he was out of doors they turned downwards, although they were apt to roll upwards if he sat for some time watching a game of tennis. Another patient remarked that she had noticed a special tendency for the eyes to turn up if she looked at a bright light. This patient told me that she found that the eyes soon resumed their normal position if she lay down.

Associated blepharospasm was observed in two of my cases, and two other patients stated that they were unable to open their eyes during an attack, possibly for the same reason. On the other hand one patient said that he was unable to close the eyes during an attack. In more than one case there were vertical nystagmoid movements. A backward movement of the head, in association with the upward movements of the eyes, was noted in one case, but I have not personally met with any instances, such as have been reported by Wimmer and others, in which there were widespread spasmodic movements of the face, limbs and trunk.

Fatigue and emotion are factors which appear to play a rôle in exciting the attacks. Thus in most of my cases the patient stated that the movements were especially apt to occur towards the latter part of the day or when he or she felt physically tired. Several patients remarked that the movements became exaggerated when attention was

directed to them, or when they felt self-conscious or agitated. Thus one girl found that her worst periods were when she sat down to a meal, while a man complained that the upward movements were most troublesome when he was in a crowd. Again, I was struck by the fact when examining one of my patients, the case in which the deviation was lateral, although this is no doubt mere coincidence, that while she was unable to maintain central fixation when asked to do so the movements of the eyes disappeared when I engaged her in conversation. Further, this patient remarked that the movements did not occur when she was reading or sewing. Hyoscine has sometimes an undoubted effect in ameliorating, and indeed may actually control, the movements.

The nature and manner of production of these movements is a question of much interest. Since they have only been observed, so far as I am aware, in association with the Parkinsonian manifestations of epidemic encephalitis, their dependence upon the same pathological process is unquestionable. It is tempting to suppose that the upward movements of the eyes may be of the nature of a release phenomenon, and that as the lateral movements are preponderatingly represented in the cortex, so in the brain-stem the representation of the vertical movements predominates. On the other hand the direction of the movements is not always upwards or downwards, while diplopia is sometimes complained of during the attacks. Again, a variety of tic-like movements of the face, tongue and jaws, are met with in these cases of encephalitic Parkinsonism. It is difficult to avoid the conclusion that an irritative process plays a prominent part in their production.

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NOTE ON THE PAIN SENSATIONS WHICH ACCOMPANY DEEP PUNCTURES.

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DURING the course of determinations of tissue temperatures [Bazett and McGlone, 1927] some hundreds of deep punctures into the tissues have been made, while in other experiments repeated venepunctures have been performed [Dreyer, Bazett and Pierce, 1920], and one of us has also been a subject for arterial puncture on several occasions. These experiments allow certain generalizations to be made in regard to the sensations experienced, particularly as to the similarity of the peculiar sensations which usually accompany arterial puncture to those which occasionally are induced by venepuncture, and which are commonly observed when a needle exerts any tension on the deep fascia. These sensations have a definite character and may perhaps help to elucidate the sensory symptoms of some neuralgias. They are also of interest in relation to the study of nerve distribution to the vessels made by Woollard [1927].

Arterial puncture.—The sensations which accompany such punctures are well recognized. When the needle reaches the vessel wall, a dull aching sensation is felt which is much less acute than is a simple puncture of the dermis; the pain, however, is much less bearable. It is diffuse, is often referred to some other position (usually one more distal), and the aching sensation is often associated with uncontrollable reflex reactions; the subject may complain of a sudden sensation of warmth, may break out into a sweat, may then feel cold, faint, or actually lose consciousness. The sensations may be accompanied by nausea, and in some individuals by a desire to defæcate. There is a similarity to the sensations experienced with testicular injuries; though the actual pain is less intense, the reflex changes of an autonomic type may be just as pronounced. As is well known, the sensations accompanying

punctures of the brachial artery are less intense than those experienced when the radial artery is pierced; this has been very noticeable in our experiments. We have had no experience with puncture of the femoral artery in the groin. In two experiments, where the puncture of this vessel was attempted with a thermocouple needle, no such sensation was experienced at all, but it remained doubtful whether the needle ever entered either the vessel or its wall.

When the muscles, and less commonly the dermis, are punctured the needle may occasionally enter a small artery; with thermocouple needles such an event may be indicated by the occurrence of bleeding along the tract (outside the needle), even when quite small needles are employed. When a vessel within the dermal area has been punctured during the introduction of a thermocouple needle (tangentially or obliquely directed), an unusual degree of pain commonly accompanies the injury, and there is produced an inflammatory hyperæmia greater than the average in area and intensity. When, however, such a hæmorrhage has occurred after the needle has pierced the deep fascia, and where the blood presumably has escaped from some intramuscular vessel, the pain has been of a dull aching character, not easily bearable, and reflex responses of the fainting type have been in evidence. In fact, if a puncture produced such intense symptoms that a needle had to be withdrawn (though introduced in a subject thoroughly inured to the procedure), indications of puncture of a deep vessel, in the form of hæmorrhage along the needle tract, was rarely absent. It seems, therefore, that puncture of the smaller vessels, with the possible exception of those in the dermis, is accompanied by more severe sensations and symptoms than is puncture of the larger vessels.

Venepunctures.—The sensations experienced are usually those of dermal puncture alone, and the vessel puncture gives no sensation. Occasionally, however, a small nerve appears to be affected (in our experience in 2 or 3 per cent. of the punctures); the sensations experienced are then similar to those of arterial puncture, but much less severe. Such sensations have been least rare when a vein has been punctured near a valve where muscular contractability and the supply of nerves might be anticipated to be maximal.

Deep punctures on the extensor aspect of the fore-arm.

Dermis.—Punctures made with a needle at right angles to the surface are accompanied with a simple pricking sensation of an acute type, which subsides at once and which is accompanied by a slight local inflammatory

reaction, but by little or no hyperæmia except in the immediate neighbourhood. If, however, the needle be introduced tangentially, the sensations are more noticeable, last longer, and an inflammatory hyperæmia may often be distinguished over an area of one or more centimetres diameter. The pain is irritating, but not nauseating. The inflammatory reaction and the pain are perhaps more marked when the needle travels parallel to the surface for some distance near the junction of the dermis and fat, but unquestionably there is a definite relationship in any one subject between the severity of the painful sensation and the degree of the inflammatory hyperæmia.

The subcutaneous fat.—A needle introduced at right angles to the surface can usually be moved back and forth in the subcutaneous fat with little or no sensation of pain; there are no unpleasant reflex responses, nor are inflammatory reactions much in evidence.

The deep fascia.—As soon as the needle reaches the neighbourhood of the deep fascia, the subject notices sensations of the type already described in relation to arterial puncture, though, when the needle is very sharp, the sensations are occasionally absent. The sensations are usually only moderately severe and appear to arise when the needle point is in close proximity to, or touching, the external aspect of the fascia; they subside rapidly once the fascia has been punctured. If, however, the needle position is such that tension is exerted on the deep fascia, or if the needle be jarred so that impulses are transmitted to the fascia, sensations may continue or return. The sensations are commonly so definite that the subject can identify the fascial plane as readily as he who introduces the needle, and a subject may faint when the fascia is touched, even though he has shown no reaction for a quarter or half an hour previously while the needle has been only in the dermis and fat.

Muscles.—Once the point of the needle is within the muscles, sensations are as a rule absent, unless tension is being exerted on the deep fascia. Intermuscular septa may, however, be encountered and can be recognized by the resistance offered to the needle. Sensations similar to those induced from the deep fascia may accompany their puncture, though they are usually much less definite. The needle may also encounter small blood-vessels with the symptoms already described. We believe we have touched or punctured occasionally the interosseous membrane in the fore-arm; this has been accompanied by symptoms and sensations similar to those produced by arterial puncture.

Periosteum.—The needles have often been introduced till they have

met the radius or ulna bones. Contact of the needle point with the periosteum usually produces sensations of a moderate severity, which closely resemble those already described in relation to arterial puncture.

Inflammatory reactions.—The inflammatory responses serve to demonstrate that the reactions are not of mere psychical origin. In most subjects puncture of the fascia is not accompanied by any marked hyperæmic reaction; however, in some subjects a diffuse hyperæmia makes its appearance as soon as the sensations of fascial puncture have been noted, but not before, even though the needle may have been in position in the subcutaneous tissue for a long time. In all subjects the painful sensations experienced when a small blood-vessel is pierced, and when the periosteum is irritated, is almost invariably accompanied by the rapid development of a diffuse hyperæmia; there is a noticeable parallelism between the severity of the sensation and the degree of hyperæmia in any one subject.

Deep puncture of the inner aspect of the thigh.—The sensations and symptoms resemble those observed with puncture of the fore-arm, except that in the one subject used the reactions following thigh puncture are greater, fascial pain is apt to be more intense, and the puncture of arterial branches with the accompanying intensified reactions seems to be more common. Most of the punctures have been made over the sartorius muscle in the middle third of the thigh. In this region several fibrous septa may be met within the subcutaneous tissue; these may give rise to sensations similar to those given by the deep fascia, but as a rule the sensations are not so marked. Puncture of the fascial plane on the deeper aspect of the sartorius muscle usually produces a definite reaction; if the needle be introduced at the edge of the sartorius muscle, where the two planes join, the needle may continue to meet with obstruction for a considerable distance, and the whole of such a puncture may be accompanied by moderately severe sensations of the type described.

When punctures have been made on the inner aspect of the thigh, just above the knee-joint over the vastus internus muscle, hæmorrhage along the needle tract and severe sensations of the type described have been more common than with punctures in a more proximal position.

Deep puncture of the external aspect of the thigh.—This has only been attempted (on the same subject used for the other experiments on the thigh) on three occasions; in every case the needle had to be removed hurriedly, soon after puncture of the fascia lata, owing to the

violence of the fainting symptoms which have accompanied the aching sensation, and the consequent danger to the thermocouple needles in use. The symptoms have been more violent than those accompanying radial puncture, and have necessitated the subject lying down for ten to fifteen minutes after the withdrawal of the needle.

DISCUSSION.

The difference in the type of pain experienced with puncture of deep fascial planes, or of a small artery, from that which accompanies dermal puncture is most marked, and the sensations resemble those of some forms of neuralgia. It has been noticeable how commonly there has been evidence of puncture of a small artery, where the subject has considered that a small nerve has been injured, and it seems probable that the sensations may arise from the nervous plexi which accompany the vessels. It is noteworthy that Woollard [1927] anticipated, from his anatomical studies, that the vessels should be sensitive and that this property should be most marked in smaller arteries and rare in the veins; this is confirmed experimentally. The association of similar sensations with puncture of the deep fascia may conceivably be associated with the presence of a plexus of arterial vessels just superficial to this membrane [Spalteholz, 1893], or to the presence of a nervous network in the same position [Ruffini, 1905].

The more marked sensations of the smaller vessels may be dependent on the greater supply of medullated nerves to these vessels [Woollard, 1927], but, if so, the relief of pain in patients with Raynaud's disease subjected to sympathectomy by Davis and Kanavel [1926] is not readily explained.

The nerve-endings in the vessel walls need not necessarily normally carry sensory impressions, since they may represent nerve-fibres utilized in vascular dilation through axon-reflexes, and hence in direct continuity with other sensory branches.

CONCLUSION.

The pain experienced when arteries are punctured is described, and comparison is made with the similar pain experienced when the deep fascia is pierced or exposed to tension, or when the periosteum is injured. The occasional pain experienced when a vein is punctured is of the same type. The sensation is that of a dull ache, not necessarily very painful, though difficult to endure and associated with reflex changes of an autonomic type, such as sweating, fainting, or nausea.

The puncture of the fascia on the outside of the thigh produces much more severe symptoms than a similar puncture of the inner side; and both produce more severe reactions than does puncture of the extensor aspect of the fore-arm.

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A CONTRIBUTION TO THE CLINICAL STUDY OF SCHILDER'S ENCEPHALITIS.

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THE morbid state first fully described by Schilder [6] as encephalitis periaxialis diffusa is now established as a disease, or perhaps as a type of disease, whose features may be recognized with certainty by post-mortem examination. We have thus reached that stage of investigation at which we can take the morbid anatomy as our criterion, and upon the foundation which it provides we may begin to accumulate and sift the clinical and ætiological data.

The basis of the present paper is provided by a case proved by post-mortem examination to have died of Schilder's disease. Its clinical interest depends upon two unusual features. The first and most important is that a sister and brother who are still alive are both suffering from an organic cerebral affection which cannot be classified under any of the orthodox disease headings, whilst of the remaining brothers and sisters, out of a total of ten, five have died at various ages from 7 months to 13 years of supposed meningitis or convulsions. Thus it would appear for the first time evidence is produced which suggests that Schilder's encephalitis may have a familial incidence.

The second point of interest is that the fatal case already referred to was correctly diagnosed during life upon clinical features which have not previously been recorded as characteristic of the disease.

Case 1.—Tommy P. was admitted to Guy's Hospital, under the care of Dr. Cameron, on October 8, 1926, aged 6, with the complaint of difficulty in walking.

It was stated that he did not walk until he was 3 years old, but from then until the age of 6 appeared normal, and went to school at the age of 4. After the death of his mother in May, 1926, it was noticed that he would sometimes sigh and make noises in his sleep, but this was put down to fretting. He continued at school until June, when he was admitted to the Rotherhithe Infirmary on account of general weakness. He was discharged after a fortnight, but readmitted from August 18 to 31. A report states that, during this period,

for the first few days, he was mildly feverish (99° to 100° F.) and was rather listless. It was noted also that at times he showed a curious sighing type of respiration. Subsequently he became steadily weaker, and by the beginning of October was unable to walk or stand.

On admission to Guy's Hospital he had a rather vacant look. Intellectually, he appeared slow. There was no aphasia. The optic discs were normal. The visual fields were full to rough tests. The pupils were equal, regular and central, and reacted normally to light and in accommodation. Ocular movements were full, but nystagmoid jerkings were seen in lateral deviation to right and left. The functions of both fifth nerves were intact. There appeared to be weakness of both sides of the face, but more marked on the left; the palate was raised to the right, and the tongue protruded to the left. The limbs showed general spasticity and weakness, especially on the left side. The deep reflexes were increased, those of the left side being the brisker. The abdominals were absent; the plantar responses extensor on both sides. There was incontinence of urine and faeces. No sensory loss could be detected. There were no abnormalities discovered in any of the other systems.

It was observed that the child had a curious smile, which developed slowly and took an equally long time to fade. The breathing was shallow and interspersed with many sharp sighs.

The rectal temperature was 99° F., pulse 110, and respiration 30.

Further investigations showed a negative Wassermann in blood and spinal fluid. The latter was clear and not under obvious pressure and showed protein 0.025 per cent., cells 1 per c.mm., slight reduction of Fehling's solution, chlorides 0.69 per cent.

No tubercle bacilli could be detected in the fluid, and cultivations remained sterile after seventy-two hours' incubation at 37° C.

The clinical picture presented, therefore, was that of a progressive double hemiplegia in a child of 6. There was no evidence of increased intracranial pressure. The advanced bilateral pyramidal signs without involvement of brain-stem nuclei suggested symmetrical disease in both hemispheres rather than a single central lesion.

Upon this basis the diagnosis of Schilder's encephalitis was therefore made and subsequently adhered to.

In view of the known tendency of this disease to involve the optic radiations, the patient's visual acuity and visual fields were subsequently examined from day to day, as well as his failing mental powers would allow. Unfortunately, no records of these tests were kept, but, in the opinion of the house physician, Mr. H. Trafford, the visual power and range remained normal up till death. The optic discs were also examined from time to time, and were observed by the writer to remain normal, and were so when the child was last seen on the day before death, which occurred on October 21.

Post-mortem examination.—The brain and spinal cord, which showed no external abnormality, were separately removed and placed in formal saline. One or two vertical cuts were made through each cerebral hemisphere so as to allow rapid and complete fixation. After hardening, the brain-stem and cerebellum were detached, and the hemispheres cut horizontally into slabs of about



FIG. 1.—Horizontal section through the right cerebral hemisphere just above the lateral ventricle. Brain of Tommy P. Formalin fixed. Unstained.



FIG. 2.—Horizontal section of right frontal lobe a few centimetres below the vertex. Brain of Tommy P. Formalin fixed. Unstained.

2 cm. in thickness. The brain-stem, cerebellum and spinal cord were accidentally destroyed before they could be examined.

Macroscopic examination of the hardened slabs at once confirmed the diagnosis of Schilder's encephalitis.

Throughout both hemispheres the white matter showed a diffuse gelatinous degeneration, most advanced in the deeper parts—where in some areas cavities had formed. Where it extended towards the cortex, the degeneration left the subcortical white matter intact, so that this layer stood out as a pale strip

between the grey degenerated area internally and the grey matter of the cortex externally (fig. 1).

The distribution of the areas of degeneration was studied by naked-eye

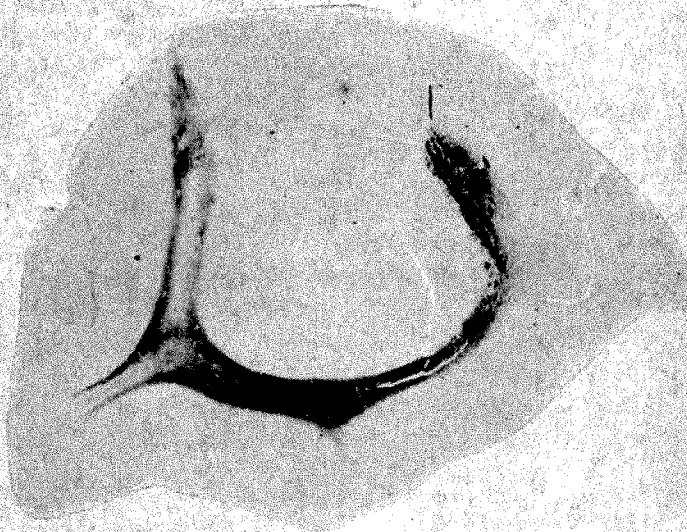


FIG. 3.—Section of the right frontal lobe. Brain of Tommy P. Stained by the Weigert-Pal method. In one part of the section even the subcortical fibres show evidence of demyelination.



FIG. 4.—Section of the left parietal lobe. Brain of Tommy P. Stained by the Weigert-Pal method. The base of the gyrus is severely involved. The demyelination extends throughout its core, leaving a relatively thick surround of well-myelinated fibres subjacent to the cortex.

examination of the serial slabs. The white matter of both frontal lobes was involved throughout their whole extent from vertex to base (fig. 2). The degeneration appeared to be of oldest standing around the anterior cornua of the ventricles, where in parts there was actual loss of substance.

The temporal, parietal and occipital lobes were relatively less affected. The white matter surrounding the ventricles was severely involved, but there were comparatively well-myelinated areas in the centrum ovale, and the white matter of the gyri in those parts did not show the same uniform and clear-cut distinction between a central core of grey degeneration and subcortical strip of normal fibres which was evident throughout the frontal lobes.

Around the posterior cornua of both lateral ventricles, however, the degeneration was more striking than in any other part of the brain, so that in the shrunken condition of the fixed specimen the neighbouring masses of grey matter formed the lips of irregular cavities from which all semblance of white matter had disappeared, except the narrow strip of subcortical fibres.

The disease was, on the whole, symmetrically distributed throughout the two hemispheres.

Microscopic examination confirmed the naked-eye impression of symmetrical demyelination, furthest advanced in degree and extent throughout the frontal lobes. Here in some areas it was difficult to obtain any positive result from the Weigert-Pal method, even the subcortical fibres taking up the stain faintly (fig. 3).

Further back (e.g. in the parietal lobes), the disease process was less advanced. The base or pedicle of the gyrus was severely involved, and the demyelination extended throughout its core, leaving however a relatively thick surround of well-myelinated fibres subjacent to the cortex (fig. 4).

Under the higher powers it was clear that there was swelling and fragmentation of fibres adjacent to the areas of complete degeneration which appeared well stained to the naked eye, and it was impossible to draw any sharp line of demarcation between the healthy and the diseased tissues.

Sections stained with Scharlach R. showed a comparable state. In the zone nearest the cortex the myelin was swollen and fragmented, and there were occasional mononuclear cells with scarlet inclusions in the perivascular spaces. Within this again there was an area in which the remnants of the myelin were represented by yellow-stained granules and droplets lying within a reticulum of swollen mononuclear cells, whilst at the base of the gyrus there were clusters of cells packed with scarlet granules.

Corresponding sections stained by Anderson's modification of the Victoria blue method for neuroglia showed in the subcortical layer an increase of glia fibrils which became thicker and more numerous towards the centre of the gyrus. In the central core was a dense felt-work of fibres running in all directions with many spider cells. Other sections stained by Busch's modification of the Marchi method provided the counterpart to the Weigert-Pal sections, showing the finger-like extension of myelin decay extending from the centrum ovale into the core of the gyrus, towards, but not reaching, the cortex.

The family history.—The father of Tommy P., aged 48, is at work in London. He has enjoyed good health, with the exception of an anthrax pustule some years ago, from which he made a complete recovery. He has had defective vision since the age of 12. It has not been possible to examine him,

The mother, who had previously had no illness of importance, died of pulmonary tuberculosis one year ago.

There have been thirteen children of this marriage, of whom two—besides Tommy—have been examined by the writer.

Concerning the remainder, the data here recorded were obtained in a personal interview with the father.

(1) The eldest child, a male, died at the age of 2 weeks, the cause of death being unknown.

(2) *Case 2.*—Nellie P., the second child, aged 20, is an inmate of Leavesden Mental Hospital, where the writer was enabled to examine her on December 18, 1926, by the kindness of Dr. R. M. Stewart, who has placed the available records of her past history at his disposal.

Her father states from memory that she never walked and was backward and invalid from birth. It was, however, recorded on her case sheet when she was admitted to the Fountain Hospital in March, 1918, at the age of 11, that she had walked at the age of 10 months and talked early. This history was presumably obtained from her mother, now deceased, and is more reliable.

On the same case sheet it is recorded that she was observed at the age of 1½ years and was backward then. From the same record it appears that on admission (aged 11) she was quite helpless, could not stand or sit alone, did not know her age or address, only knew two colours, blue and red, and made no attempt to describe a picture even with help. The note on the physical condition is: "Fair condition, somewhat thin, lower limbs crippled, hand and fore-arm apparently contracted." The circumference of the skull was 20 in.

From this time forward she was under institutional care as an imbecile. Occasional notes of her physical condition record that in February, 1919, "she talks to other children and is remarkably observant. No grip to her fingers." In April, 1921, "on account of all her limbs being crippled she makes no headway, talks readily and is fairly intelligent." In April, 1922, when she was transferred to Leavesden Hospital, the report is: "She is an imbecile without epilepsy. Cannot read or write; can only count up to ten; can recognize simple objects. She is in poor general health, feeble circulation in extremities. Cerebral diplegia; extensor paralysis of fore-arms; spastic paralysis of lower limbs." In February, 1925, the first note is made of her vision: "She is blind and quite helpless, but shows a fair amount of intelligence. Her answers to questions are childish and often irrelevant."

There is no record of her ever having had any epileptic attacks. Her father thinks that her eyesight was normal when she left home in 1918, and that she has only become blind in recent years.

The following notes were made by the writer on December 18, 1926:—

Nellie P., aged 20, admitted Fountain Asylum, 1918. Examined with Dr. R. M. Stewart, December 18, 1926.

From nurses.—She will converse in a childish way with them and with other patients. Takes food slowly out of a spoon, has no dysphagia. Knows

where she is. Recognizes people by their voices. Can see a little. Has not changed much in last year or so, except that she has become more faulty in her habits. No epilepsy.

Examination.—On hearing strange voices became agitated and distressed, crying and shrieking for Nurse Mabel, and saying, "Go away." Articulation clear; voice strong. Can distinguish light from darkness. Told by nurse that the visitors were gone, she said "Go away" when I flashed an electric torch in her face. Optic discs pale and clear cut; the appearance of primary optic atrophy. Pupils dilated and do not react to light. Divergent strabismus, but no definite ocular paresis detected. No nystagmus. Right face weaker than left as she cries. Sensation not examined for want of co-operation.

Motor system: As she lies in bed the head is somewhat retracted, but this is less evident when she is sat up; and it is difficult to distinguish between resistance and true rigidity. The upper limbs are symmetrically fixed in the following position: Adduction at the shoulders. Extreme flexion at the elbows. Extreme pronation at the wrists. Extreme flexion at the wrists and metacarpophalangeal joints. Extension of inter-phalangeal joints. Adduction of thumbs. The rigidity appears to be of the clasp-knife type, but voluntary resistance and contracture make examination difficult. There is apparently no voluntary power; but handling the limbs produces flexor spasms. No wasting.

Trunk: Nothing abnormal noted.

Lower limbs: Both semiflexed at hips, and knees and ankles with toes flexed and curled downwards.

Reflexes: Tapping upper limbs provoked some clonic spasms of biceps. Abdominals not elicited—but interfered with by crying. In the lower limbs tapping produces clonic spasm of calf muscles; no other reflexes obtained.

Sphincters: Wet and dirty.

General physique.—Head and trunk normally developed. Pubic hair normal. Limbs small as in an infantile hemiplegia, with cyanosed extremities. Extreme pyorrhœa. Liver and spleen not felt. Kyphosis of lumbar spine. Chest not examined on account of struggling.

(3) The third child, Freddie P., died recently at the age of 18, of pulmonary tuberculosis.

(4) The fourth child, a girl, is said to have died of meningitis at the age of 13 months. No clinical data available. No autopsy.

(5) Lily P. is said to have died of meningitis, aged 13. No clinical data. No autopsy.

(6) Jessie P., aged 15, is alive and well and keeps house for her father.

(7) *Case 3.*—William P., aged 11, was first admitted to Guy's Hospital at the age of 3, when notes were made of his condition, and has been under the observation of the writer for the past five years.

As an infant he developed normally; but he began to suffer from fits at the age of 2, this being attributed at the time to a slight head injury. Subsequently there were convulsive attacks at irregular intervals. According to the mother, these would usually begin with twitching of the right face, arm

and leg, the convulsions would then become generalized and the patient would lose consciousness.

He was first admitted to Guy's Hospital in April, 1919, during one of his attacks, which had begun as usual with right-sided convulsive movements. On admission he was unconscious, but quickly recovered.

Under observation he was thought to be mentally backward and nervous. No localizing signs were found, and he was discharged with the diagnosis of Jacksonian epilepsy.

He was readmitted in July, 1919, and was said on this occasion to have had a left-sided Jacksonian attack. On this occasion he was seen by Mr. H. L. Eason, who noted defective vision, especially in the lower fields, and optic atrophy. The Wassermann was negative in the blood. The diagnosis of cerebral tumour, unlocalized, was made, and he was discharged.

Following this, he had no more attacks until September 14, 1922. On that day there was a series of convulsions, each beginning with twitching of the right angle of his mouth, spreading over the right side of the face, subsequently affecting the right arm and leg. He was admitted unconscious during one of these attacks. On the next day (September 15, 1922) the fits had ceased, but he was still unconscious. The deep reflexes on the right side were increased and the right plantar response extensor. On the 16th he was conscious, but remembered nothing since going to bed on the 14th. The reflexes were as before.

The writer saw him for the first time on September 22, 1922, and made the following notes:—

Cerebration: Odd, over-active. Speech: normal.

Special senses: Vision: acuity very fair to rough tests. Fields: some peripheral constriction, especially on right. Discs white and clear-edged, some pigment disturbance around, vessels a fair size, cups not very distinct. I think a primary atrophy.

Cranial Nerves: Pupils dilated with atropine, neither eye turns in very well on conjugate deviation. Slight weakness of right face on emotional movement, otherwise normal.

Sensation: No defect of sensation.

Motor System: Left grip better than right, but says he is left-handed.

Reflexes: All tendon-jerks present and equal on the two sides. Abdominals upper and lower present and equal on the two sides. Plantar responses: right doubtful, left flexor.

Sphincters: No disturbance of sphincter control.

Gait: Walks on a rather wide base and is unsteady.

Impression: Cerebro-cerebellar atrophy.

He was again admitted in February, 1925, and was then reported to have had mild fits once a fortnight, or oftener, since his discharge from hospital in 1922. The account given by his mother was that on these occasions, if playing in the street, he would run inside and lie down; after a minute or two, twitching would begin in the right side of the face and extend to the arm and leg; this would continue for a few minutes; after that he would feel quite well

again and ready to go out to play. Consciousness was not always lost in these attacks. On the day of admission an attack of this kind was followed by a series of fits, during one of which he was admitted. Chloroform was given to control the convulsions, which subsided, leaving him dazed and confused. He was discharged ten days later.

Following this, the fits continued at irregular intervals, but lost their Jacksonian character and became generalized. The story now is, that he is found unconscious, having fallen down.

He was readmitted in December, 1926, for a month's observation, during which he had one brief attack; he was heard to grunt but, by the time the nurse reached his bed, there was no convulsive movement and he appeared dazed, but was not unconscious.

On examination the physical signs were as before. Physically and mentally he is underdeveloped, and the optic discs show primary atrophy with general constriction of the fields. An occasional extensor response can be obtained on both sides; otherwise there are no abnormal physical signs.

The Wassermann is negative in blood and spinal fluid. The spinal fluid contains no excess of protein or cells. X-ray pictures of the skull show no abnormality.

(8) The eighth child, sex unknown, is said to have died of meningitis, aged 7 months. No clinical data or autopsy.

(9) The ninth child, sex unknown, is said to have died of convulsions, aged 9 months. No clinical data or autopsy.

(10) Tommy P. is the case of Schilder's encephalitis recorded above.

(11) A boy, said to have died at nine months of meningitis.

(12) Alfred, aged 3, is said to be alive and well.

(13) Irene, aged 18 months, is said to be alive and well.

DISCUSSION.

The clinical diagnosis in the case of Tommy P. rested mainly upon the exclusion of other possibilities.

The indubitable signs of bilateral pyramidal involvement without any nuclear palsies or other evidence of brain-stem lesion indicated disease of both hemispheres. The absence of any headache, papilloedema, vomiting or hydrocephalus was against the diagnosis of tumour. The normal cerebro-spinal fluid excluded meningitis. These points having been made, the gradually progressive course of the illness suggested a subacute encephalitis. Encephalitis lethargica had then to be considered, but the steady progressive evolution of the disease and the clinical picture of pyramidal involvement were against this. Of known cerebral diseases, therefore, Schilder's encephalitis provided the only satisfactory diagnosis.

It was noteworthy that the visual fields appeared intact, but account

was taken of the cases in which the disease was recorded as having commenced in the frontal lobes (Jakob [3], Walter [8], Kaltenbach [4]).

Comparison of the brain of this case, both in its macroscopic and microscopic appearances, with the descriptions of other writers—especially those of Collier and Greenfield—leaves no room for doubt in the writer's mind as to the pathological diagnosis.

The question next arises whether the other two members of this family who are suffering from obscure encephalopathies may be included clinically within the bounds of Schilder's disease, as already described by other writers.

In the case of William P. the symptoms are mental retardation, epileptic attacks and optic atrophy. All these symptoms have been described by various authors in proved cases of Schilder's encephalitis.

An additional feature of this case, however, is the apparent arrest of the disease; for during the past five years, while he has been under the writer's close observation, there has been no evidence of its progress, and from the history it is probable that his condition had been stationary for three years before this.

This, however, is no new conception in the story of Schilder's disease. The case reported by P. Marie and Foix in 1914 [5] was that of a girl who was taken ill at the age of 18 with a rapidly progressive quadriplegia reaching its height on the fifteenth day of the illness. Subsequently there was some improvement and she remained in a stationary condition for ten years. She then died—not of an exacerbation of the original disease, as erroneously quoted by Collier and Greenfield [1]—but of pulmonary tuberculosis.

The pathological appearances were characteristic of the disease now known as Schilder's encephalitis, save that the microscopic detail was that of an old-standing lesion.

In a recent paper, Foix and J. Marie [2] again draw attention to this case, and record two others comparable in the points of clinical arrest and pathological scar. One was a boy triplegic, blind, epileptic and imbecile, who died at the age of 14, the brain showing the typical central, symmetrical, grey degeneration with sparing of the subcortical fibres. Clinically his condition had apparently remained stationary since the age of $4\frac{1}{2}$.

The other case, even more striking, is that of a man, aged 65, who was said to have had convulsions at the age of a few months, leaving as their sequel a spastic right lower limb with equinovarus and extensor

plantar response. Post mortem a patch of sclerosis was found in the left centrum ovale; its relations with the paracentral lobule explained the clinical picture. The lesion showed the typical extension into the gyri with sparing of the subcortical fibres.

P. Marie and Foix [5] named the condition which they originally described centrolobar sclerosis. Foix and J. Marie [2], adhering to this term, consider that it represents a pathological picture distinct from that described by Schilder only in so far as centrolobar sclerosis may be regarded as a late or healed stage of encephalitis periaxialis diffusa.

The conception of the disease held by Foix and J. Marie [2] is that it is subacute in its onset and progress, but not necessarily fatal. It may thus leave its victim crippled with a healed scar, or scars, in the white matter of the hemispheres.

This conception opens up new fields for exploration. The whole group of spastic diplegics or hemiplegics, whose symptoms date from a history of convulsions or other nervous illness in infancy but are not progressive, deserves to be re-investigated on the pathological side. The morbid anatomy of these conditions has never been satisfactorily classified, and it is possible that the appearances now recognized as typical of Schilder's disease might not have been apparent to the unaccustomed eye.

The story of Nellie P. raises further possibilities. Her present state of spastic quadriplegia, imbecility and optic atrophy, suits well with the diagnosis of Schilder's encephalitis. The occurrence of optic atrophy, now several times reported in proved cases of the disease, must depend, as Stewart, Greenfield and Blandy [7] point out, upon its distribution, and is therefore as much an accident of localization as the occipital blindness with normal pupillary reactions which has been such a striking feature of other cases.

Taking the history on the case record to be correct, and assuming that Nellie walked at 10 months and talked early, the clinical symptoms of the disease must have appeared at the end of her first year and have progressed fairly rapidly, in that she was observed at the age of 18 months and was backward then.

It seems, however, both from the case records and the observations of the parents, that the disease has been gradually progressive throughout the whole period of nine years during which she has been under institutional care. For in 1918 there is mention only of hand and fore-arm contracted; in 1919 there is no grip to her fingers; in 1921 all her limbs are crippled but she is fairly intelligent. In 1922 she can

recognize simple objects (presumably visual recognition). In 1925 she is blind. Her father is certain in his own mind that the loss of vision has been a development only of recent years.

If, then, this case is to be regarded as an example of Schilder's encephalitis, we shall have to add a chronic progressive type of the disease to our list of clinical varieties.

SUMMARY.

A case of Schilder's encephalitis is described in which the diagnosis was made during life and proved post mortem.

The family history of this case shows that, of the twelve brothers and sisters, one died in infancy from unknown causes; one died in adult life from pulmonary tuberculosis; three are alive and well; five died in infancy or childhood from causes notified as "meningitis" or "convulsions" without further evidence of the clinical or pathological state. The other two, a girl aged 20 and a boy aged 11, present symptoms of cerebral disease which are described. These symptoms are, it is suggested, compatible with the clinical diagnosis of Schilder's encephalitis.

Evidence is thus produced which suggests that Schilder's encephalitis may have a familial incidence.

I have to thank Dr. Hector Cameron for permission to record the case admitted under his care, and Dr. J. Godwin Greenfield for his invaluable assistance and advice.

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A CONTRIBUTION TO THE PATHOLOGY OF HEMICHOREA.

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Most of the authors dealing with the problem of the choreic syndrome have adopted Wollenberg's ætiological classification of its different clinical manifestations. A more recent minor modification is that of Lotmar [4], who divided them into three groups:—

(1) The chronic progressive form, hereditary, with progressive dementia = Huntington's chorea.

(2) The infectious and toxic form.

(3) Macroscopic, localized lesions which may involve the cerebellum, the anterior cerebellar peduncles, the red nucleus, the body of Luys, the thalamus or the striate body.

C. and O. Vogt [6], [7], tried to correlate the clinical syndromes with pathological entities. According to their classification of extra-pyramidal diseases, the following structural changes will produce chorea:—

(1) Progressive status fibrosus of the striate body.

A. Without severe degeneration of the pallidum and the correlated mid-brain nuclei. Clinically: Progressive bilateral chorea.

(a) If this process is localized in the striate body it will reveal itself clinically as isolated chorea.

(b) If connected with a diffuse necrosis of ganglion cells in the rest of the brain, especially those of lamina IV of the cortex, the clinical picture of Huntington's chorea is produced.

(c) As subsyndrome of general paralysis: Chorea combined with other symptoms of general paralysis.

B. Combined with severe disease of the pallidum: Chorea with subsequent rigidity.

¹ Presented at the Annual Meeting of American Neuropathologists' Club, Atlantic City, N.J., May, 1927. From the Neuropathology Laboratory, Montefiore Hospital, New York.

(2) Status subinflammatorius (encephalitis).

A. Encephalitis of unknown origin in striatum. Clinically: The progressive striate syndrome.

B. Encephalitis epidemica. Clinically: The striate and pallidum syndrome.

C. Sydenham's chorea with a predilection for the striate body. Clinically: Chorea.

(3) Macroscopic, localized vascular disease in the striate body of adult people. Clinically: Hemichorea.

Cases of the last group should help us in solving the problem of the localization of the different forms of extrapyramidal disturbances of motility. As has been mentioned above, such macroscopic localized lesions may involve any part of the cerebellum-nucleus ruber-thalamus-striatum-pallidum pathway, and produce the clinical picture of hemichorea. C. and O. Vogt presented among their material only one case with vascular lesion of the striate body associated with hemichorea. Case 34 (Liepmann's case, Elizabeth L.):—

An unmarried woman, aged 42, was transferred to an insane asylum because of hallucinatory dementia. At 67 she suffered from an attack of hemichorea which first involved the right face and arm, and five months later also the right leg. The tendon reflexes were very lively at this time. Two years later, two weeks before death, the patient had a left-sided hemiplegia. From the case report it may be concluded that there was a slight degree of rigidity. Marked arteriosclerosis of the cerebral vessels was found. The head of the caudate nucleus and the oral part of the putamen were replaced by an old cyst, which also had partly destroyed the anterior limb of the internal capsule.

A second case is briefly mentioned by Jakob [2]:—

Sudden onset of choreic movements in the right face in a case of psychosis of arteriosclerotic origin. Anatomically, the cystic remains of softening in the ventral and oral part of the head of the left caudate nucleus were found.

A third case of vascular lesion of the striate body with hemichorea was reported by Lloyd and Winkelmann [3]:—

A patient with a right hemiplegia of three years' duration developed a left hemichorea three weeks before death. Anatomically: Generalized arteriosclerosis of the brain was reported. An old focus of thrombotic softening was found in the left internal capsule, and another focus of more recent origin in the right hemisphere which involved a narrow strip along the inner margin of the putamen, but extended into the outer portion of the globus pallidus. The internal capsule was involved to a very small degree in its

posterior portion by a hæmorrhage, which impinged upon the corpus Luysi and extended into the pes pedunculi. Both striate bodies were atrophic and showed poverty in medullated fibres, especially on the right side. Both thalami contained multiple areas of softening and hæmorrhage. The nucleus ruber and substantia nigra were normal.

A fourth and a fifth case belonging to this group are found in the French literature. Case 4, reported by Austregesilo and Galotti [1], was that of a left hemiparesis with right hemichorea. Anatomically: An irregular focus of softening was present in the head of the left caudate nucleus, with complete destruction of the nervous tissue and new formation of many capillaries. The internal capsule and the rest of the brain were intact.

Case 5 is that of Souques and Bertrand [5]:—

A woman, who died at the age of 54, had suffered at 4 years of age from an infectious disease, which was followed by a left hemiplegia and a left hemichorea. Contractures and a positive Babinski developed. Anatomically: A degeneration of part of the right putamen and the caudate nucleus was found. The anterior part of the corpus callosum was destroyed. The corona radiata showed paling of its upper part in myelin-stained sections, and destruction of fibres in its deeper layers. The anterior third of the posterior limb of the internal capsule was involved, and the anterior peduncle of the right thalamus was also cut by an area of degeneration. The pallidum I was affected in its external and posterior third. The body of Luys was atrophic and almost unrecognizable.

The rarity of localized macroscopic vascular diseases in the striate body with hemichorea may justify the report of the following case:—

M. L., aged 58, a Russian Jew, married at the age of 35, and had seven children, all living and well. In 1911, at the age of 43, patient was suffering from diabetes mellitus, which never attained a severe degree during the following eight years. In 1919, amputation of the second toe of the left foot and of the first phalanx of the second toe of the right foot was performed. In June, 1926, patient complained of general weakness and severe pain in the toes. On August 13, 1926, he was admitted to the Post-graduate Hospital, where, on August 20, slight twitching movements of the right face were noticed. These movements rapidly spread to the right arm and shoulder, and later, increased in intensity and involved the right leg. On September 20 they had attained such an intensity as to become alarming. On October 5, 1926, the patient was transferred to Montefiore Hospital.

Neurological examination.—Constant twitching and grimacing of the right side of the face. Eye muscles normal. Pupils irregular, right larger than left; sluggish reaction to light, but normal contraction on accommodation. The left corneal and conjunctival reflexes are sluggish. There is a slight drooping of the left angle of the mouth. The uvula deviates to the left; the pharyngeal reflex

is absent. The tongue deviates to the left, but is not tremulous. The right arm is held in adduction, the elbow in flexion, and the hand in partial flexion with fingers contracted. The frequent movements of the arm are jerky in character and choreiform, while the movements of the right hand and fingers, like those of the facial muscles, are often slower and worm-like. There is atrophy of the intrinsic muscles of both hands, more marked on the right. The muscular power of the right arm is diminished; the patient is unable to raise this limb. There is no fixation in the right leg; wasting is present in the

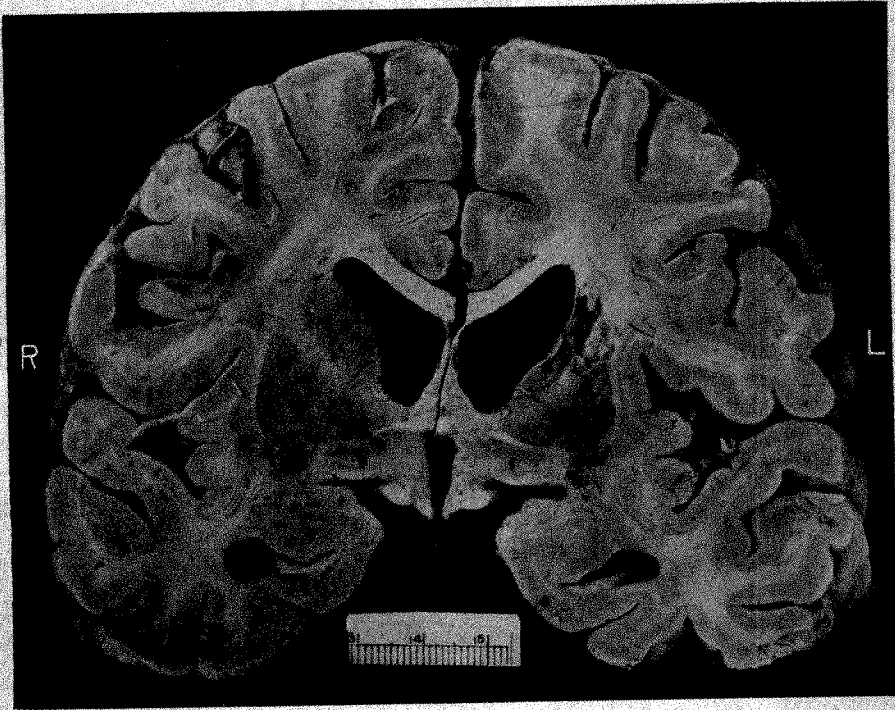


FIG. 1.—Vertical section through brain at the level of the anterior commissure. Cyst formation with destruction of part of caudate nucleus, putamen and internal capsule on left side.

muscles in both legs, more pronounced in the feet, but muscular power is not diminished and both legs can be raised. The movements of the right leg are jerky. The tendon reflexes are absent on the right side, present on the left. There are no signs of involvement of the pyramidal tract. The abdominal reflexes could not be obtained on admission, but on October 25 they were present on both sides, but more lively on the right. Proprioceptive sensations were absent in both lower extremities. Vibratory sense was greatly diminished below the eleventh dorsal root area, and there was hypæsthesia and hypalgesia below the first lumbar area. The mental state was normal. Spinal fluid



FIG. 2.—Vertical section through brain. Loyez stain. Atrophy and demyelination of left striate body and pallidum.

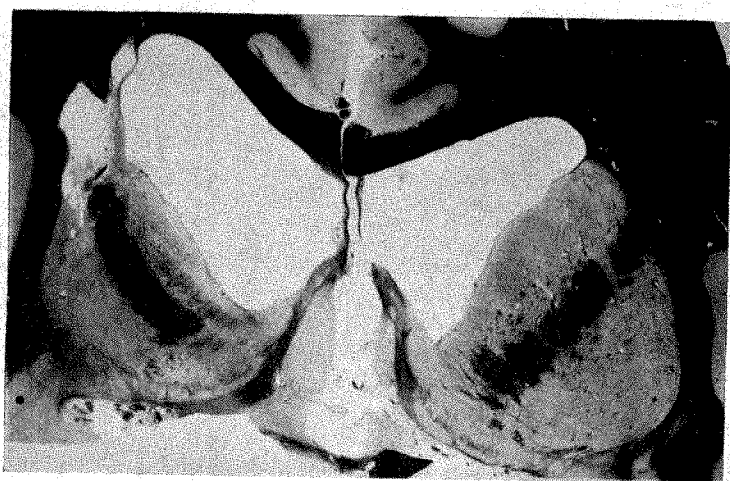


FIG. 3.—Microscopical vertical section through brain, approximately 15 mm. frontal of figure 1. Loyez stain. Cyst formation with partly destroyed striate body and internal capsule

contained 20 cells, a trace of globulin and sugar 4 plus. Blood-sugar was 170 mg., and the blood-pressure 200/90.

Course of the disease.—On November 3 a gangrene of the right second toe

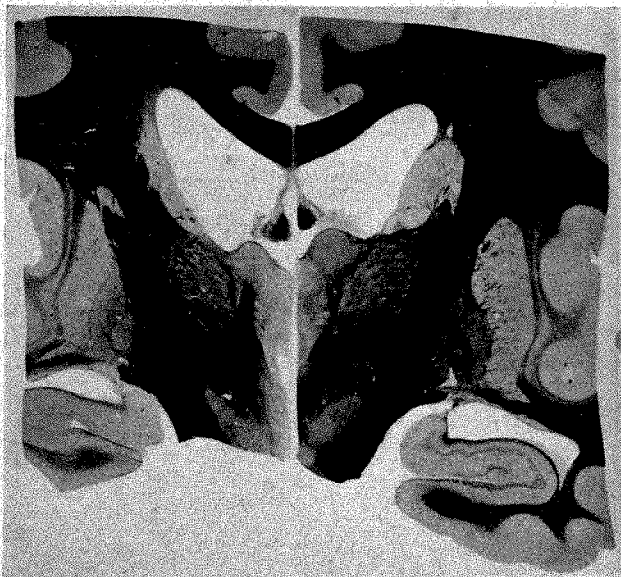


FIG. 4.—Microscopical section through brain, approximately 3 mm. occipital from mammillary bodies. Loyez stain. Atrophy and demyelination of left striate body and pallidum.

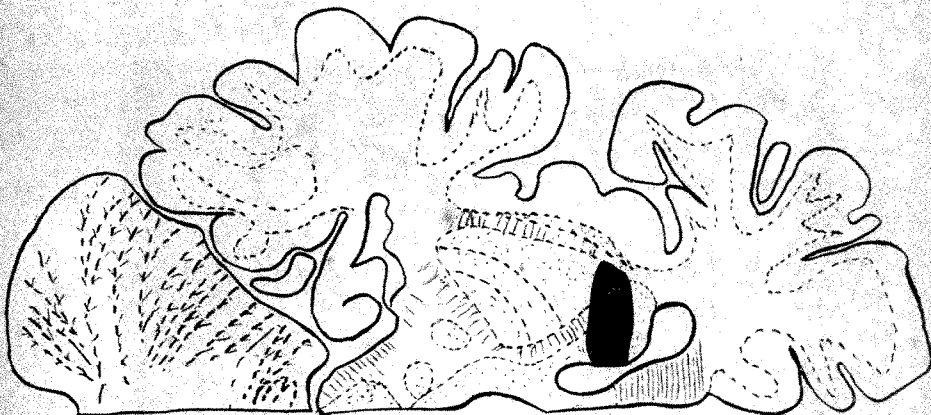


FIG. 5.—Diagram of horizontal section through brain to show approximate extension of cyst in anterior-posterior direction.

developed, first dry, then moist and spreading. On January 1, 1927, amputation of the right lower leg had to be performed. Patient died on January 12, 1927, from pneumonia.

Anatomical report.—Leptomeningitis at the convexities of the brain, with

arteriosclerosis of medium degree of the vessels at the base. The left side of the cerebellum is smaller than the right; the vessels covering the left cerebellar hemisphere are not as prominent as those on the right side. The brain looks smaller than normal, but weighs 1,100 grm. The convolutions throughout are slightly atrophic. The lateral ventricles are enlarged, the left more than the right. There is a cyst formation with destruction of nearly the whole anterior third of the left caudate nucleus, approximately the upper third of the anterior limb of the internal capsule and the upper part of the oral pole of the putamen (fig. 1). The remaining parts of the left striatum and left pallidum are reduced in size. The corresponding basal ganglia and the thalamus on the right side appear normal. In sections through the whole brain stained by Loyez' method, the atrophy of the left striatum and pallidum is still more evident (figs. 2, 3, 4). Drawings were made of these nuclei at a linear enlargement of 1:9, and their planes were measured in corresponding sections of both sides with the planimeter. The following table gives the averages of twelve measurements, corresponding to sections taken from the neighbourhood of the section shown in fig. 4. The numbers indicate square inches at a linear enlargement of 1:9:—

TABLE.

	Plane in square inches		Planimetric index		Left nucleus in per cent. of right
	Right	Left	Right	Left	
Caudate nucleus ..	5.760	3.484	26.3	26.9	60.6 per cent.
Putamen ..	11.254	6.216	51.5	48.0	55.5 "
Pallidum I ..	3.328	2.272	15.2	17.5	68.0 "
Pallidum II ..	1.598	0.982	7.0	7.6	64.4 "
Total ..	21.870	12.954	100.0	100.0	59.2 "

(The planimetric index indicates the percentage of the plane of a given nucleus as compared with the total sum of the nuclei of the same side. Example: The planimetric index of right caudate nucleus is $\frac{5.760 \times 100}{21.870}$.) This table indicates that the relative sizes of the different nuclei on the right or left sides are approximately the same, but all the nuclei on the left side are smaller than those on the right side. The left putamen is largely involved in this atrophic process, while the left pallidum I showed only a reduction of one-third of its plane as compared with the right side.

One section through the cerebellum was measured in order to determine the approximate degree of the deviation between the right and left sides. These are the perimeters which were found: Visible surface, right 12.5 cm., left 12.25 cm.; difference 3 per cent. Total surface, right 68.8 cm., left 61.7 cm.; difference 10 per cent. These differences are within normal limits and do not indicate an atrophy of one half of the cerebellum as compared with the other half.

Histological report.—Sections of the spinal cord stained by Loyez' method show a pallor of the inner half of the posterior columns at the level of the lower dorsal segments, with reduction in the number of myelin sheaths. The walls of the blood-vessels in this region are thickened and their lumina reduced.

Arteriosclerotic changes of medium degree are found in the pons, the ventral half of which was more involved.

There are no striking histological changes in the cerebellum. The nucleus ruber and substantia nigra on both sides are normal. The left body of Luys is richer in glial nuclei than the right, and its ganglion cells contain more pigment, which enlarges the cells and forms globule-like appendices. In Loyez-stained sections the inferior part of the capsule of the body does not stain as well as the rest; the fibres forming the tract which connects the outer part of pallidum II with the mid-brain nuclei (*faisceau pallidal de la pointe*) are less numerous than in the corresponding right sections. The lateral nucleus of the left thalamus is rich in glial cells, and its ganglion cells show different degrees of atrophy; they are more darkly stained by Nissl's method, and many of them are completely broken down. The dorsal and the medial nuclei of the left thalamus appear normal. The right globus pallidus shows no striking changes. In the left pallidum II there is scattered perivascular oedema with some round-cell infiltration, but the ganglion cells are not markedly affected.

A similar picture was seen in the left pallidum I. Towards the putamen there is an increase in the number of glial nuclei and in the number of diseased ganglion cells. In the striate body these histological changes reach their maximum, and the process of degeneration involves both large and small cells. In the oral part numerous gitter cells replace the broken down tissue, which is partly intermingled with connective-tissue fibres. Fat stains show numerous granules in the glial and ganglion cells. Iron stains reveal granular cells laden with iron pigment, and the left striate body and pallidum stain more bluish than the right side. Glial stains reveal a preponderance of microglia in the region of the left striatum in the proximity of the lesion. In sections stained by Loyez' method the right basal ganglia are coloured distinctly darker, and contain more myelinated fibres than the corresponding left nuclei (fig. 4).

COMMENT.

On comparing the five cases published previously with the present case, it appears that the hemichorea affected only persons older than 50 years of age (Jakob does not state the age of his patient), who were suffering from arteriosclerosis of the brain. In the cases of Vogt, Jakob, Austregesilo and Galotti, and Souques and Bertrand, and in the present case, the oral part of the caudate nucleus and putamen was destroyed by a cyst formation; in the case of Lloyd and Winkelmann the lesion was more occipital and did not affect the caudate nucleus. Unfortunately, neither Vogt, Jakob or Austregesilo and Galotti give detailed histological reports which would allow a further comparison of the six cases. Lloyd and Winkelmann state that the lesion also involved the thalamus and the body of Luys on the right side. Besides, they found "a generally medullary fibre poverty in the striatum, particularly on the right, with

a generalized atrophy." In the case of Souques and Bertrand, the deeper layers of the corpus callosum were destroyed, as well as the anterior third of the posterior limb of the right internal capsule and the anterior peduncles of the right thalamus; pallidum I and the body of Luys were also affected.

In studying Plate XXVII, figs. 3 and 4, of Vogt's case [6], the left caudate nucleus and the visible part of the left putamen seem to be smaller than the corresponding right nuclei. In the present case there was a marked atrophy with poverty in myelinated fibres in the whole right caudate nucleus, putamen, both pallida and the body of Luys. It is evident that in Lloyd and Winkelmann's case, and in my own, this general atrophy of basal ganglia and the diminution of fibres cannot have been secondary to the lesion which produced the hemichorea, but must have preceded the extrapyramidal disturbance. In Lloyd and Winkelmann's case the choreiform movements appeared only three weeks before death, in the present case five months before. Further, in the cases of Lloyd and Winkelmann, Souques and Bertrand, the body of Luys was involved; in my case this nucleus was smaller than the right and richer in glial nuclei. The inferior part of its capsule was poorly developed, and the fibre tracts connecting the pallidum with the body of Luys and the substantia nigra on the left side showed a diminution of myelinated fibres. In these three cases part of the thalamus was also involved in the pathological process.

Localized lesions of the striate body are very frequently encountered without clinical signs of hemichorea. Jakob already emphasized the complexity of the problem, and pointed out that cases of localized lesions of the striate body which are combined with hemichorea are extremely rare compared with the relative frequency of such lesions found at autopsy. He thought that other pathological changes in the motor apparatus and "individual conditions" must be combined with such striate lesions in order to produce the choreic syndrome. He did not, however, express an opinion as to the nature of such accessory conditions.

The lesions known to produce hemichorea may occur, as stated at the beginning of this paper, in the anterior cerebellar peduncle, in the thalamus, in the neostriatum and in the body of Luys. It appears that lesions in any part of the sestructures may eliminate a path the integrity of which is necessary to the absence of chorea. Lesions of the cerebello-rubral system do not produce chorea, nor do lesions of the thalamo-cortical fibres. In the cases of Lloyd and Winkelmann, Souques and

Bertrand, and my own, the lesions involved at the same time the external nucleus of the thalamus, the anterior limb of the internal capsule, the striatum and the body of Luys.

Beyond describing the various parts of the path—anterior cerebellar peduncles, thalamus, striatum, body of Luys—and the lesions which were found in this case, no conclusions can be drawn, and it is felt that conclusions which state that the lesion which causes hemichorea must lie in a specific part of this path, are, at present at least, premature.

Conclusions.—Localized macroscopic vascular lesions of the striate body in adult people do not produce the clinical picture of hemichorea. They have to be associated with more generalized histological lesions of the striatum, the pallidum, thalamus, or the body of Luys. In the present case of right hemichorea, a cyst formation in the oral part of the left striate body was combined with hemiatrophy of the whole left striatum, the left globus pallidus, the left body of Luys. The histological picture showed increase in glial nuclei and poverty in myelinated fibres in the atrophic nuclei. There was also found sclerosis of ganglion cells in the lateral nucleus of the left thalamus.

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TRIGEMINAL NEURALGIC PAIN ASSOCIATED WITH MULTIPLE SCLEROSIS.¹

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SEVERE protracted pain in cases of multiple sclerosis is so rare that it seems hardly worthy of discussion. However, during the course of a long series of cases of multiple sclerosis four were noted in which the patients complained bitterly of intense paroxysmal neuralgic pain localized in one or more divisions of the fifth nerve. To these unfortunates pain seemed to be the most important complaint in their disease, and they demanded relief regardless of what else could be done to ameliorate their general helplessness. Accordingly, these cases stand out in bold relief from the general run of cases of multiple sclerosis and as such demand some inquiry.

Similar cases have been described by competent observers and in at least one instance careful necropsy suggested causes for the pain. Oppenheim reported the case of a patient suffering from multiple sclerosis whose early yet permanent symptom was severe neuralgic pain in the area of the fifth nerve. The patient died, and at necropsy a plaque was found on the root of the fifth nerve at the zone of its entrance into the pons. A drawing of a microscopic section of the pons appears in Oppenheim's textbook of nervous diseases. Marburg found the same pathological changes in a similar clinical case, and Berger, in a study of 206 patients suffering from multiple sclerosis, noted in the case histories of two that severe paroxysmal trigeminal neuralgic pain had been present at some time during the course of the disease. In one of these cases the pain was the initial symptom, and it had persisted from the beginning of the disease, a period of five years. Gullain noted the presence of neuralgic pain in the area supplied by the fifth nerve in two patients at the beginning of the disease. Unfortunately, the foregoing observers did not give enough detail with regard to the type of pain observed. In most instances it

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was described as neuralgic and paroxysmal, but the symptoms were not subjected to the minute scrutiny that modern clinical experience has demanded for the purpose of classification.

REPORT OF MAYO CLINIC CASES.

Case 1.—Multiple sclerosis of twenty years' duration: Disease far advanced and all symptoms well marked. Paroxysmal trigeminal pain for six years in the left second divisional area without any objective sign of injury to the fifth nerve: Section of the posterior root: Complete relief from pain, but death four days after operation: Necropsy.—A man, aged 44, was brought to the Mayo Clinic, April 15, 1923, complaining of paralysis of the limbs and pain in the left side of the face. Twenty years previously he had noticed that in running his lower limbs felt heavy and stiff, and that he raised them from the ground with difficulty. Later he noticed that his gait had become so unsteady that he staggered in walking. With periods of remission and exacerbation he gradually became worse, so that eleven years before examination he required assistance to walk. Finally he was unable to walk at all and for five years his lower limbs had been completely paralysed.

Thirteen years previous to examination the patient had noticed tingling in the right hand and it had become difficult for him to write. His hand was unsteady, awkward and clumsy, and for eight years he had been unable to feed himself. The left arm became affected about two years after the right, but never to the same extent, and he was still able to feed himself with it although it was unsteady and clumsy. Fifteen years previously incontinence of urine appeared; this progressed to the stage of complete loss of control. Bowel control had remained normal. Transitory diplopia, lasting two to three days at a time, had appeared eight years before.

Six years previously the patient had experienced, for the first time, sudden, sharp, stabbing, shooting pain in the left cheek, localized in a small area. These paroxysms lasted only thirty to sixty seconds. At first single paroxysms occurred, with freedom for from three weeks to several months. Later many paroxysms appeared close together and lasted for hours and the remissions became shorter. The pain was extremely severe; it usually came on in the morning and was initiated by talking, chewing or washing the face. The patient remained as quiet as possible during attacks lest a paroxysm occur. The pain remained unilateral, but, whereas at first it occurred in the left cheek only, later it occurred in the left side of the nose and left upper lip, but was confined to the area supplied by the second division of the fifth cranial nerve. A year before he came to the Clinic three deep alcohol injections had been given within two weeks. Relief lasting for two months followed. A series of three injections were then given, with relief for four months. Thereafter the pain had become more severe, the paroxysms more frequent and the area involved greater. Eleven days before examination an alcohol injection had been given without any result whatever. On the morning of examination an

attack lasting an hour occurred. Each paroxysm lasted half a minute and was repeated every few minutes.

Examination.—The patient was emaciated, bedridden and obviously suffering severely. Between attacks, however, he was euphoric, happy and cheerful out of proportion to his affliction. His intelligence was somewhat low, but he co-operated readily and efficiently in the examination as far as pain would permit. Horizontal and vertical nystagmus and weakness of conjugate movement of the eyes to the right was noted. Vision was not reduced and the optic discs seemed normal. There was spastic paralysis of both lower extremities and of the right upper extremity. The left upper extremity was weak and spastic also, but to a much less degree, although there was marked incoördination in the finger-to-nose test. All tendon reflexes were exaggerated and the plantar reflexes were in extension. Abdominal reflexes were absent. There was diffuse diminution of pain and thermal sensibility, variable in degree and extent, over both lower extremities and over the abdomen up to the eighth dorsal segment. Joint and vibration sensibilities were markedly reduced in the four extremities. Speech was scanning in character. There was no anæsthesia or motor paralysis in the area of the fifth nerve, but the slightest stimulus applied to the left cheek or left side of the nose was enough to induce a severe paroxysm of pain. Talking, eating or laughing also caused pain, and altogether the patient's general behaviour was similar to that of a patient suffering from major trigeminal neuralgia. The urine contained a great deal of albumin and pus and a considerable number of red blood-cells. The Wassermann tests on the blood and spinal fluid were negative. The Nonne test of the spinal fluid was positive; there was one small lymphocyte for each cubic millimetre, and the colloidal benzoin curve was 000000333300000. There was an area of sloughing over the sacrum from decubitus.

Treatment.—Because of the patient's suffering, which interfered with the last remnant of enjoyment of life, section of the posterior root of the left fifth nerve was advised. April 20, 1923, under general anæsthesia, this operation was performed by Dr. Adson. The patient's immediate post-operative condition was good and he was free from pain for four days, when he suddenly became cyanotic with rapid, shallow breathing and feeble pulse. He died within an hour.

Necropsy.—Apart from the observations on the central nervous system, to be later discussed, the more important changes discovered were enormous dilatation of the stomach, chronic inflammation of the bladder with trabeculation and diverticula, moderate arteriosclerosis, emaciation and decubitus. The immediate cause of death was assumed to be acute dilatation of the stomach.

When the skull was opened gross signs of meningitis were not present. The operative field apparently was not infected and there was no more hæmorrhage than would be expected following such an operation. The posterior root of the left Gasserian ganglion had been completely severed close to the central end of the ganglion. The brain, spinal cord, and the right and left Gasserian ganglia with their posterior roots were removed, and also the peri-

pheral branches of the fifth nerve as far as it could be reached by the intracranial route. These tissues were immersed in formalin, and after they were satisfactorily fixed and hardened an endeavour was made to establish the diagnosis of the disease in the central nervous system, and to estimate, as far as possible, its anatomical distribution. The cerebral hemispheres were separated from the brain-stem by section through the upper part of the mesencephalon, and the cerebellum was detached by severing its peduncles. Coronal sections were made through the cerebral hemispheres. In the white matter in each section innumerable greyish plaques, varying from minute specks to 4 or 5 mm. in diameter, were clearly visible to the naked eye. These were scattered irregularly throughout the white matter, but were more numerous in the neighbourhood of the lateral ventricles. In the subependymal layer of the ventricles were translucent grey areas about 8 mm. thick, following closely the contour of the ventricular cavities and chiefly in the region of the posterior and inferior horns. Only a few plaques were found near the third ventricle and the cortical grey matter was comparatively free.

Microscopical examination of the isolated plaques and those confluent in the ventricular wall illustrated the following characteristics. With a modified Weigert myelin-sheath stain the plaques were completely demyelinated and stood out as white sharply outlined circular areas on a black background. Many of the plaques surrounded a central blood-vessel. With higher magnification the myelin sheaths appeared to end more or less abruptly in the margin of the plaques, with here and there a solitary nerve-fibre still retaining its stain crossing the dead white area. With Bielschowsky's and Orlando's stains the axis-cylinders in the plaques were relatively unaffected and continued on their course across the margin of the plaque into its centre. With Weigert's neuroglia stain there was an obvious increase in glial fibres, so there was a dense felting more marked toward the centre. Study of the central blood-vessel present in some of the smaller plaques showed some of the perivascular spaces filled with compound granular corpuscles, which when stained with Scharlach R. were found to be loaded with fat granules. Areas lining the walls of the lateral ventricles were merely a confluence of innumerable plaques with the characteristics described. Altogether the histology of the plaques was identical with that described in multiple sclerosis, and such was the final pathological diagnosis.

Sections were made of the spinal cord and medulla at various levels and stained with Weigert's myelin-sheath stain. Numerous plaques, scattered indiscriminately, were found along the course of the spinal cord. There was rather marked degeneration of the pyramidal tracts in the dorsal and lumbar regions. In the upper cervical spinal cord and lower medulla a plaque was found in the spinal root and nucleus of the fifth nerve on the right side (fig. 1). This, however, disappeared at a level corresponding to the upper third of the inferior olive.

Serial sections, 20 micra thick, were made of the pons throughout its extent and every fifth section was stained with Loyez' modification of Weigert

myelin-sheath stain. Sclerotic plaques of various sizes were found in every section, but the largest was that in the floor of the fourth ventricle, occupying nearly its whole length and breadth. Opposite the main sensory nucleus of the fifth nerve and on the right side there was a tongue-like projection of the plaque which enveloped this nucleus as well as the fibres of the

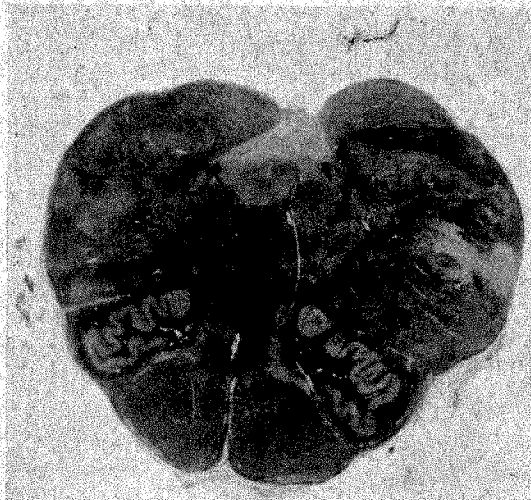


FIG. 1.—Section through the medulla in the region of the inferior olive showing plaque on the descending root and the nucleus of the right fifth. ($\times 4.5$.)

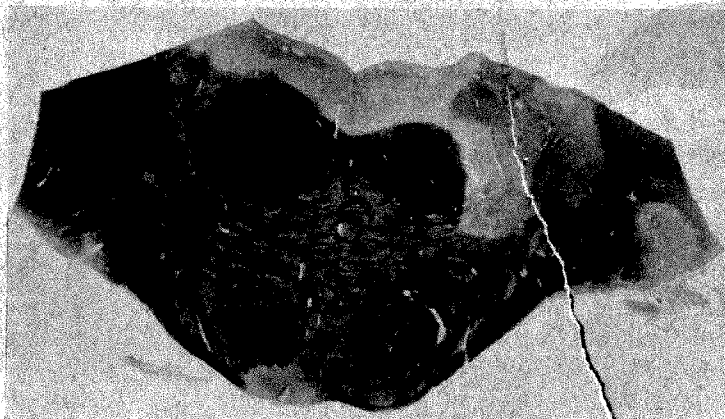


FIG. 2.—Section through the middle of the pons showing a large plaque in the region of the nuclei of the right fifth nerve and its descending roots. The floor of the fourth ventricle is occupied by a large plaque. Numerous larger and smaller plaques in other areas of the section. ($\times 4.5$.)

median fillet on that side. The nuclear cells, however, seemed intact although surrounded by sclerotic tissue. The left fifth nerve nucleus was intact (fig. 2).

Both roots of the fifth nerve were traced upward in their oblique, outward course within the pons; they emerged in the usual manner and formed the posterior root of the nerve. As traced upward each root took the myelin stain well and did not seem at all degenerated, but just at the point of emergence of the left root two plaques appeared and engulfed its fibres. On the right side the root seemed normal (fig. 3). Study of the left root in its extrapontine course showed that the sclerotic process extended outward a short distance within its substance, and then the root became seemingly normal again up to the point of its severance by the surgeon, at which point it was surrounded by a blood-clot. Study of the left Gasserian ganglion with various stains (Weigert myelin-sheath, van Gieson, hematoxylin and

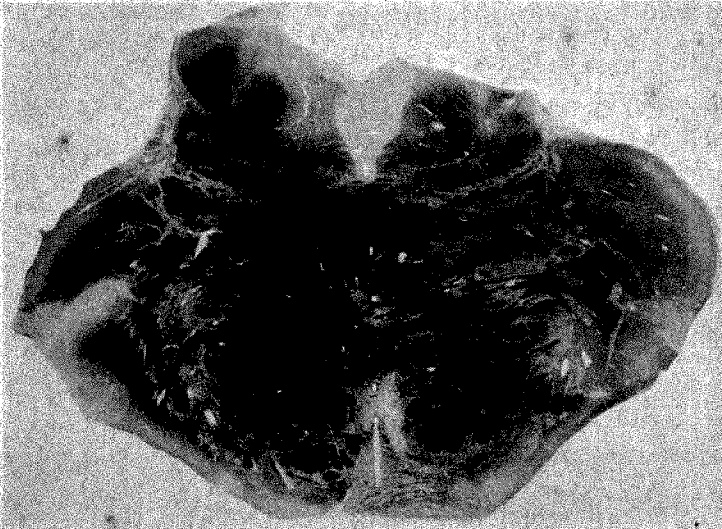


FIG. 3.—Section through the pons at the level of the emergence of the left trigeminal nerve root. Two plaques are to be seen invading the emerging fibres of the root. The right fifth nerve root at this level is normal. Numerous smaller plaques scattered throughout the section. ($\times 4.5$).

eosin, and Nissl's stain) showed nothing more than could be attributed directly to the trauma of surgical intervention. The ganglion was sectioned serially and scrutinized minutely for sclerotic plaques but none were found. Hæmorrhage was found on one surface, and a mild inflammatory reaction was present close to the hæmorrhagic area. The ganglion cells, however, were normal in size, the nuclei were central and the pericellular capsules intact. The blood-vessels were normal and unusual pigmentation was not present. The intraganglionic nerve-fibres took the myelin stain well, and neither the entering root-fibres nor the issuing nerve-trunks showed frank evidence of degeneration. The right Gasserian ganglion and corresponding posterior nerve-root were normal in all respects. Studies of the mid-brain

showed relatively few plaques, and the mesencephalic root of the fifth nerve on each side was apparently normal. The cerebellum was comparatively free, except for one large plaque about 2 mm. in diameter in its white matter near the nucleus dentatus and roof of the fourth ventricle.

Summary of necropsy findings.—The disease of the central nervous system from which the patient suffered was multiple sclerosis. Innumerable plaques were scattered throughout the brain and spinal cord. Well-marked and relatively old plaques were found on the main sensory nucleus of the right fifth nerve. On the right side and on the lowest part of the spinal nucleus and root was a plaque. The right posterior root was normal, but on the left side at the point of emergence of the root from the pons and for a short distance along its extrapontine course, there were two relatively old sclerotic plaques. The Gasserian ganglia and the central portions of the peripheral nerve-trunks were free from any sclerotic process.

Comment.—The case was one of typical slowly progressive, well-developed and well-established multiple sclerosis. Whatever doubts might exist with regard to the clinical diagnosis the observations at necropsy establish beyond question the nature of the disease. The condition had existed for twenty years and was readily recognized, but for six years pain had been present identical to that described under the synonyms of tic douloureux, trifacial neuralgia and major trigeminal neuralgia; none of the features of the latter disease was lacking. The pain was lancinating, paroxysmal and distinctly confined to the second divisional area of the fifth nerve. The paroxysms, occasionally spontaneous, usually were initiated by moving or touching the face or jaws. Accordingly, during certain attacks eating and drinking were avoided and the patient's nutrition suffered. The usual periods of remission had occurred, and on two occasions the injection of alcohol into the trunk or peripheral branches of the fifth nerve brought relief for a few months. In spite of the severity of the sclerotic process in the pons, no objective or subjective signs of injury to the fifth nerve were present, apart from the paroxysmal pain.

From a review of the clinical history of this one case, and without the necropsy data, it might be assumed that two distinct disease entities were present in one patient at one and the same time, namely, multiple sclerosis and trigeminal neuralgia. It could have been argued that the presence of a pain syndrome identical with trigeminal neuralgia in a case of multiple sclerosis was a mere coincidence of two unassociated diseases. However, the experience of this patient as well as that of three other patients similarly afflicted, tends to suggest some causal relationship between the multiple sclerosis on the one hand and the trigeminal pain on the other.

Case 2.—*A nine-year history of multiple sclerosis with well-marked signs and symptoms; a three-year history of paroxysmal trigeminal pain in the second divisional area on the left side; no relief from alcohol injections into the infra-orbital nerve; section of posterior root of the fifth nerve and complete cessation of pain.*—A woman, aged 39, first came to the Mayo Clinic, October 7, 1918. She had complained then of difficulty in walking. Thirteen years previous to this visit she had first experienced transitory diplopia. This recurred four years later and at this time also there appeared divergent strabismus of the left eye, formication and hyperæsthesia over the left side of the face, dropping of the left angle of the mouth, tinnitus in the left ear, and extreme vertigo with vomiting. These symptoms came on within two or three days and with fluctuations; they disappeared within a few months. Five years before examination weakness in the left lower extremity with a tendency to drag the limb in walking had developed. This reached its maximum in six months and then gradually disappeared. Two years previously this trouble had recurred, gradually developing within a space of two or three months. This time the patient did not recover but became worse, and the right lower extremity became affected also. Her gait had become stiff, slow and unsteady. She dragged her limbs as she walked, particularly the left side.

Examination.—The general physical examination showed a somewhat emaciated woman unable to walk without assistance. Ophthalmoscopic examination of the fundus showed slight pallor of the optic discs, more marked on the left side, but vision was $\frac{20}{20}$ in both eyes. Marked sustained nystagmus, both vertical and horizontal, was present. There was no facial weakness, but the left eye could not be closed without the right participating. There was general increase in tone, loss of speed, and weakness in all extremities. The weakness was slight in the upper limbs but reached the degree of a marked spastic paresis in the lower. All tendon reflexes were increased, more markedly on the left side. Babinski's sign was present on both sides. Abdominal reflexes were absent. There was marked movement tremor in the upper and lower extremities, and in walking there was a coarse, general tremor. If the patient attempted to stand with her eyes closed and feet close together she swayed and fell and the general tremor was again obvious. There was slight diminution of pain and thermal sensibilities over both extremities, but in all other areas, including that supplied by the fifth nerve, sensibility was normal. There was no involvement of the motor division of the fifth nerve. There was no disturbance of joint, vibratory or deep pain sensibility. The gait was spastic, more marked on the left side, with the general tremor mentioned. Speech was normal, and sphincteric control was normal. The Wassermann tests on the blood and spinal fluid were negative. The Nonne test on the spinal fluid was negative and there was only one small lymphocyte in each cubic millimetre. A diagnosis of multiple sclerosis was made. The patient was not seen again for six years.

The patient again visited the Clinic, August 21, 1924, because of paroxysmal pain in the left side of the face. Three years before this second visit

she had an attack of paroxysmal sharp shooting pain in the left cheek. All her teeth had been extracted and the pain disappeared for a year. It returned, however, and for two years preceding the second visit attacks had occurred periodically every few months until three months previously, when they remained without remission. The sudden, sharp, severe pain was confined to the left cheek and the upper and lower gums. It lasted only a few seconds and was accompanied by a burning sensation at the left angle of the mouth. The pain ceased between paroxysms. Many paroxysms were spontaneous, but most of them were initiated by touching or washing the left side of the face. Talking, chewing, laughing or drinking, or even opening the mouth, also brought on the paroxysms. The patient had been unable to eat a sufficient amount of food and therefore had lost weight. The pain was confined to the area supplied by the second and third divisions of the fifth nerve. The paroxysms came on every few minutes, and the frequency seemed to depend on physical activity, being further apart during immobility of the face, tongue and jaws. A week previous to the second visit alcohol had been injected into the left infra-orbital foramen and nerve, without relieving the pain. It produced, however, a numb sensation in the area supplied by this nerve; immediately prior to the injection there had been no paræsthesia in the painful area. So far as the multiple sclerosis was concerned the patient had not become much worse. Moreover, she had had a normal pregnancy and delivery during the period between the two visits. The child had apparently developed normally and was four years of age. In the meantime, however, the patient had been unable to walk without holding to objects and then only for a few yards.

Examination.—The patient was in poor general condition, weighing only 101 lb. as compared to her normal weight of 158 lb. She was obviously suffering extreme paroxysmal pain, and she refrained from even the slightest movement of face or jaws, fearing further suffering. Profuse lachrymation occurred during a paroxysm. Vision in the right eye was $\frac{5}{6}$ and in the left $\frac{6}{6}$. Ocular movement in all directions was slightly limited, and vertical and horizontal nystagmus was marked. There was pallor of the temporal part of the right optic disc, and all the signs of simple optic atrophy were present on the left side. There was slight weakness of the left lower lid and angle of the mouth, and well-defined hyperæsthesia to pain, tactile and thermal sensation over the left cheek, in the region of the infra-orbital foramen, presumably the result of the recent alcohol injection. The patient insisted that previous to the injection the sensation in the cheek had been normal. The symptoms noted at the neurological examination were the same as on the examination seven years previously, but further advanced. Spastic paraplegia was still present, and now the patient could not stand without support. The arms were spastic but not to the extent of the lower extremities. The movement tremor was more marked and the voice was slow and monotonous. The sphincters had remained intact.

Treatment.—A deep alcohol injection into the fifth nerve was given August 25, 1925; the second division was injected superficially August 27.

and 28. Since these injections afforded but slight relief, regional and ether anaesthesia was administered on August 31, and the sensory portion of the posterior root of the left Gasserian ganglion was cut, leaving the motor-root intact. The patient's convalescence was uneventful and she was completely relieved from pain. The usual post-operative anaesthesia of the area of the fifth nerve was complete.

Two years after the operation the patient wrote that she was free from pain in the face and consequently had gained in weight. So far as the other difficulties were concerned she was still unsteady in her gait and required assistance to get around the house, but her general comfort and happiness were greatly increased.

Case 3 — A five-year history of multiple sclerosis with all signs well advanced, three and a half years of paroxysmal trigeminal pain, first in the third division later spreading to the second, section of the posterior root with complete relief for six years.—A man, aged 34, came to the Mayo Clinic April 1, 1919, complaining of difficulty in walking and pain in the right side of the face. He had been well up to three years previously, when he had noticed progressive unsteadiness of gait and weakness of the lower extremities. He staggered and stumbled when walking, and it had become more and more difficult to start urinary flow. Sexual power had diminished. For eighteen months he had suffered from attacks of pain in the lower jaw, lasting a few hours, then disappearing for several months. The pain was sudden, sharp and paroxysmal, and radiated along the ramus of the jaw into the right temporo-mandibular articulation. During attacks, talking, eating, drinking, cold draughts, or any touch on cheek or chin initiated a paroxysm. Therefore, he was scarcely able to eat, and subsisted on semi-solid foods that did not require chewing.

Examination.—The patient appeared to be fairly well nourished. He walked with a stiff and unsteady gait. The left optic disc was slightly pale. There was moderate spasticity of the lower extremities, and their tendon reflexes were exaggerated; ankle-clonus and Babinski's sign were present bilaterally. Abdominal reflexes were absent. Vibration and joint sensibility were disturbed in both lower extremities, but there was no change in pain, tactile or thermal sensibility. Incoordination was definite and marked in both lower extremities, and the gait was ataxic and spastic. At this time he could walk unaided. In the upper extremities also incoordination was definite, but more marked on the left. He swayed when he stood with both feet together and with his eyes closed, and he could not balance himself on one foot. The Wassermann tests on his spinal fluid and blood were negative. The Nonne test on his spinal fluid was positive, and there were fifteen small lymphocytes to the cubic millimetre.

The patient came to the Clinic again, August 17, 1921, two years after his first visit, and five years after the onset of the disease. He had become very much worse so far as his walking power was concerned. Paroxysms of pain were more severe and more frequent, and the pain had spread to involve the cheek and upper jaw as well as the lower jaw. Remissions between attacks

were shorter. He had been unable to keep up his nourishment and had lost considerable weight and strength.

The patient was undernourished and, whereas before there was only slight pallor of the left optic disc, it was now quite marked and there was loss of substance in the nerve-head, with signs of beginning simple optic atrophy. However, vision was not greatly reduced in either eye. He was then unable to walk without assistance and his legs were much more spastic and ataxic than they had been. Abdominal reflexes were still absent and ankle-clonus and Babinski's sign were even more marked. The left arm remained incoördinate but not more so than previously. There was now almost complete absence of vibration sensibility in both lower extremities, and the joint sensibility of the toes was more impaired. At no time were there any objective signs of injury to the fifth nerve. On the previous visit the patient could walk, now he was almost bedridden. Trouble with the bladder became more serious, and cystoscopic examination revealed a trabeculated bladder and cystitis. The Wassermann tests on the blood and spinal fluid were again negative, and as before the Nonne test was positive and the small lymphocytes had increased, this time being seventeen for each cubic millimetre. Two deep alcohol injections were given six days apart with only temporary relief for a few hours.

While the patient was under observation, the right arm in turn became weak and incoördinate, and nystagmus and a movement tremor of both upper extremities developed. In spite of this he was distinctly euphoric when he was not suffering, but the pain became the dominant feature of his illness. It was sudden, sharp and severe, and was released by the slightest stimulus applied to the areas supplied by the second and third divisions of the right fifth nerve. It was confined strictly to those areas and was always paroxysmal; it interfered with nutrition and sleep to such an extent that with his other troubles he seemed to be slipping away. It seemed advisable, therefore, to relieve his suffering by surgical means, even in the face of the diffuse central nervous system disease.

Treatment.—September 20, 1921, under general anaesthesia, Dr. Adson cut the posterior root of the right Gasserian ganglion. The patient was relieved from pain; he gained weight and his general condition improved. With the usual optimistic euphoric personality, freedom from pain seemed to be the patient's highest desideratum, even though everything else that made life worth living were lost forever. He left for home November 21. The last communication received from him was dated February 17, 1927, that is, six years after the operation. He had never had any of the old pain, but he was much more helpless and gradually losing the use of his arms also. All he could manage to do was to sit up in his wheel-chair; he could not turn over in bed or feed himself or even light his own pipe. On the other hand, he appeared well, ate well and enjoyed food, and complained little.

Case 4.—*Multiple sclerosis proceeding with characteristic remissions and exacerbations for fourteen years; twelve years of paroxysmal pain in all three*

divisions of the left fifth nerve. Later, similar but milder pain in the right side; relief with section of the left posterior root and deep alcohol injection of the right fifth nerve; seven years later the patient was free from pain on the left side, but pain on the right had returned.—A woman, aged 42, came to the Mayo Clinic, August 14, 1920, complaining of pain in both sides of the face and unsteady gait. Fourteen years previously, following childbirth, she had noticed numbness in the fingers and a sense of unsteadiness in gait. These symptoms fluctuated considerably at the onset, with periods of improvement followed by exacerbations. There was a general tendency to get worse, and during two years previous to her visit to the Clinic the unsteadiness of gait had become permanent and she was unable to walk without assistance or support. Twelve years before examination sudden sharp, lancinating pain had developed in the left lower jaw radiating to the left temporo-mandibular joint. This spread to include the left cheek, temple and forehead. The pain usually was paroxysmal, coming on in attacks and lasting from ten days to three weeks. The paroxysms lasted only for from thirty seconds to two minutes, and were initiated by peripheral stimuli, such as talking, laughing, chewing, or washing the face. The remissions became shorter so that at the time of examination the pain appeared almost daily in the entire area of the fifth nerve on the left side. Five to seven years previously the same type of pain had commenced in the right cheek and temple. It was infrequent, not as severe as that on the left side, and only occasionally was produced by washing the face.

Examination.—The patient was undernourished and suffering from severe intermittent and paroxysmal pain in the left cheek, temple, forehead and jaws, with complete freedom between paroxysms. She appeared to dread moving any part of the affected area. There was nystagmus in all directions and a markedly ataxic gait. The lower extremities were slightly spastic, and all tendon reflexes were exaggerated with ankle-clonus. Babinski's sign was present on both sides, and Oppenheim, Mendel-Bechterew, and Chaddock signs were also present; there was, however, no marked weakness of the limbs. Abdominal reflexes were absent. There was slight incoordination of the upper extremities and marked incoordination of the lower. Sensory changes were not manifest. The function of the fifth nerve was normal, apart from the pain and the reaction to superficial stimuli. Sphincteric control was normal. The Wassermann tests on blood and spinal fluid were negative, and in the spinal fluid the cell-count was one lymphocyte for each cubic millimetre.

Treatment.—On account of the patient's obvious suffering a deep alcohol injection of the fifth nerve on the right side was given on September 1. This relieved the pain on the right side completely. The posterior root of the Gasserian ganglion on the left side was severed by Dr. Adson under general anæsthesia on September 11. Complete relief from pain followed, and at the time of the patient's dismissal, September 25, she was free from all suffering. Her general strength and weight had consequently improved. Her gait and ataxia, of course, remained the same. She was last heard of, March 26, 1927, nearly seven years after the operation. The pain on the left side had not

returned, but on the right side, where alcohol had been injected, pain had returned two months after her dismissal. Apparently it was infrequent and not severe enough greatly to interfere with her comfort. The course of the multiple sclerosis had been up and down without at any time reaching the stage of causing complete helplessness. At the present time she is still able to get around, but, of course, with difficulty.

DISCUSSION.

These four cases present many similarities, both in the course of the disease and in its salient features. In each case the disease was so well established that three out of the four patients had had symptoms for twenty, nineteen and thirteen years respectively. The disease had begun, as it usually does, in early adult life. In the remaining case the onset had occurred at least five years prior to operation. In all, therefore, the signs of the disease were well-marked and established the diagnosis of multiple sclerosis beyond any reasonable doubt. It is of interest that two of the patients were observed over a period of years during the course of the disease. In all four the course had been the usual one of remissions and exacerbations. A complete physical examination was made in each case, including a routine neurological examination, spinal puncture and laboratory tests of the blood and spinal fluid. Possibly the unusual features of the disease led to a more careful and cautious appraisal of each case. Finally, necropsy was possible in one case in which the patient died following operation, and the conditions noted in the central nervous system after death were in accord with the previous clinical diagnosis of multiple sclerosis.

The pain syndrome in all four cases was identical, and without exception it followed the course of that in major trigeminal neuralgia, with the usual remissions and exacerbations of the latter. In three of the cases the pain was unilateral, in one both sides were affected. In Case 4 the three divisional areas were affected, in Cases 1 and 3 the second and third divisions were affected, and in Case 2 the second division alone. In the cases in which more than one division was affected the pain had commenced in the second or third division and spread to the other in the course of time. The patients' sleep was not greatly disturbed, but they dreaded the periods of activity enjoined by their daily needs and preferred to remain immobile lest an agonizing paroxysm be initiated. Periods of freedom from pain were common but they grew progressively shorter, and patients were ready to accept the operation of section of the posterior root of the fifth nerve as a

source of palliative relief, even though it brought no hope of cure of other complaints.

The relation of the period of pain to the whole course of the disease varied in the four patients; two patients, who had symptoms of multiple sclerosis for nearly twenty years, suffered from pain only in the last few years. Two patients had had pain almost from the onset of the disease. One of the latter had had symptoms of multiple sclerosis for fourteen years and during twelve of these had suffered recurring attacks of paroxysmal trigeminal pain.

The resemblance of the pain syndrome in these cases to that in trifacial neuralgia led to the same surgical measures being advised as in the latter disease. So far as relief from pain is concerned, the operations were uniformly successful, since the three surviving patients have been free from pain to the present time, representing periods of two, six and seven years respectively. Alcohol injection of the nerve afforded temporary relief in a few instances, but to a much less degree. The justification for the major operation on these unfortunate patients is shown in their letters, wherein they all expressed gratitude for their relief, even though their other symptoms remain and their existence is necessarily crippled and disabled.

Pain in various parts of the body during the course of multiple sclerosis has been described by numerous authors, notably Oppenheim, Nonne, Berger, Müller, Barré, Schlesinger, Taylor, Keschner and Malamud, and Sittig. It is their common belief that pain is a somewhat rare phenomenon, but nevertheless occurs in a small percentage of cases. It seldom dominates the clinical picture, yet it may be the initial symptom and persist almost throughout the course of the disease. The pain is described variously as burning, lancinating, fulgurating, shooting, neuralgic, squeezing and lightning. Occasionally it may be severe and persistent. Müller has used the term *sclerosis multiplex dolorosa* for some of these cases. Certain observers believe that the pain originates in plaques in the posterior columns, but a greater number believe that it originates in the posterior roots. However, the correlation of symptoms in multiple sclerosis during life with the pathological changes after death has been generally recognized as a difficult task. Taylor in particular has emphasized this; in one of his cases in which severe pain has occurred in the lower extremities it might have been expected that involvement of the dorsal nerve-roots would have been observed at necropsy, but unhappily such involvement could not be demonstrated microscopically. The reverse holds also, in that marked involvement of

areas of the neural axis by the sclerotic plaques may have no clinical counterpart during life. Oppenheim had found plaques continually in relation to the fifth nerve nucleus without disturbance in the sensibility of the face; on the other hand, he has assumed that the sclerotic plaque on the fifth nerve-root was the cause of the severe neuralgic pain from which his patient had suffered. It is therefore only with caution that any assumption can be made as to the possibility of one or the other sclerotic lesion being the sole cause of the symptoms in a given case. My experience in the one case which came to necropsy was identical with that of Oppenheim as to its clinical and pathological features. It is a temptation to regard, as he did, this lesion on the posterior root as the source of the patient's pain, especially when it is remembered that so far as could be ascertained the Gasserian ganglion and peripheral branches of the fifth nerve were normal. In this regard the question arises as to whether this entrance zone of the posterior root into the pons is a particularly dolorogenetic area. Certainly the posterior roots in the spinal canal are extremely sensitive, as any surgeon can vouch for who has extracted a particularly large cord tumour while the patient was under a local anæsthetic. Touching or manipulating the roots when they are insufficiently infiltrated with the anæsthetic produces sudden darting, lightning-like excruciating pain.

Again, there is ample pathological evidence to show that compression or irritation of the root of the fifth nerve by tumours of the cerebello-pontine angle will produce intense paroxysmal neuralgic pain in the face and jaws. The cases of Lexen, Krause, and Weisenberg are good examples of this, as is a similar experience observed by me, wherein the pain produced by a tumour of the cerebello-pontine angle was identical with that associated with tic douloureux. It is also worth while to mention the former theory of Redlich and Obersteiner as to the initial lesion in tabes dorsalis of the central nervous system. This was assumed to be at the point of entrance of posterior root-fibres into the dorsal columns of the spinal cord and at the point where they lose their neurilemmal sheaths. One of the earliest symptoms of tabes is the characteristic, sudden, paroxysmal, sharply localized lightning-like pain that may appear in the face as well as in the more usual site, the lower extremities.

Any discussion as to the site and mechanism of the pain in the four cases recorded here can be made only in a spirit of pure speculation. It is manifestly impossible to form conclusions that are convincing and free from criticism since there are so many possibilities of error. I

have attempted, therefore, only to demonstrate objective data, and my interpretation of these data should be accepted in the spirit in which they are offered. My observations of these four patients may be of some interest to those concerned in the problem of the causation of pain in general, and of that referred to the fifth nerve in particular. Our clinical experience is so far ahead of our knowledge of structural change that the mechanism of the production of many well-recognized clinical syndromes lacks explanation. Pain in particular is a purely subjective phenomenon, and presents some of our most baffling problems. My experience as well as that of others seem to establish the fact that it may occur in the trigeminal area as one of the rare symptoms of multiple sclerosis, but the essential mechanism must be studied further.

CONCLUSIONS.

(1) Patients suffering from multiple sclerosis may experience trigeminal neuralgic pain. While this symptom is comparatively rare in the disease, when present it may dominate the subjective clinical picture, and may appear early.

(2) The pain may resemble closely the type complained of in cases of major trigeminal neuralgia, and it is relieved by the same surgical procedures.

(3) Four cases of well-advanced multiple sclerosis and persistent paroxysmal trigeminal neuralgic pain were studied. One patient died, and at the necropsy the diagnosis of multiple sclerosis and the distribution of the disease were established.

(4) Plaques were found on the entrance zone of the posterior root in the pons on the side affected by pain. Smaller plaques were found on the spinal trigeminal root of the opposite side in the lower part of the medulla and upper part of the cervical spinal cord. The main sensory nucleus on the opposite side was also affected, but no apparent symptoms were produced. Both Gasserian ganglia were free from sclerotic processes.

(5) The interest in these cases centres equally on the mechanism of production of paroxysmal trigeminal pain, and the fact that this type may occur in cases of multiple sclerosis.

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ADDENDUM.

After the proofs of this paper had been corrected and it was ready for press, the article of Dr. Wilfred Harris, in vol. 50, p. 403, of this Journal appeared. He mentions having seen twenty-three cases of trigeminal neuralgia associated with chronic spastic paraplegia. He considered that the majority of these patients were in all probability suffering from multiple sclerosis. In several of these patients neuralgia was bilateral. The neuralgic pain was of exactly the same type as that seen in ordinary tic douloureux or paroxysmal trigeminal neuralgia. There was no objective evidence of damage to the fifth nerve.

THE NARCOLEPSIES.¹

BY S. A. KINNIER WILSON.

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INTRODUCTION.

IN recent years attention has been directed in increasing degree to the problems presented by disorders of the function of sleep. For this, neurology has been influenced largely though in no wise solely by the world-spread of epidemic encephalitis since 1918—a morbid condition characterized in a great majority of instances by disturbance of that function. Yet interest in questions bearing on the physiology and pathology of sleep is far indeed from being a new development in neurological science. So much is this the case that not a few recent communications dealing with the subject are reduced in value by ignorance or neglect of previous work of the same kind, or along the same lines; clinical syndromes are described as new when as a fact they

¹ A paper read at the Annual Congress of the Association of Physicians, Belfast, June 3, 1927.

are very old, and hypotheses are being evolved which suffer materially, even fatally, from failure to take all the germane data into consideration.

No one with any knowledge of the facts will be inclined to deny that this is patently the case in respect of what has been called narcolepsy—a term that has always been loosely employed, various writers having described clinical examples of sleep disorder under this heading without staying to define the sense in which it is being used. As a consequence, current ideas are uncommonly fluctuating where narcolepsy is concerned, though, as we shall see, attempts at delimitation have recently been made. A legitimate matter for discussion is whether, in point of fact, clinical instances of disorder of sleep are now occurring with greater frequency than in other times. This is evidently the opinion of Brailovsky [5], who says: "In der Literatur der letzten 3 Jahre finden wir ebenso viele Arbeiten über dieses Thema wie in den vorhergehenden 20 Jahren zusammen. Sicher steht das in Zusammenhang mit der von uns durchlebten Zeit." The statement, however, is inaccurate; long before epidemic encephalitis appeared many investigators had interested themselves in narcolepsy and cognate problems of sleep, as any one who makes himself familiar with the older literature (which is far indeed from being scanty) can readily realize.

My own experience in this respect may be given a passing allusion. I was house physician to the late Sir William Gowers at the time (1907) he wrote his fine little volume on "The Borderland of Epilepsy," included in which is a chapter devoted to some sleep symptoms—among them, so-called narcolepsy. I became familiar at that time with the subject and was on the constant look-out for clinical illustrations; yet in twenty years I saw no clear and impressive example (with one or two minor exceptions), until in the course of the last few months I have at length met with four striking instances of the former, the details of which are duly recounted below. Spiller [82] appears to have had an analogous experience; writing in 1926 he says: "A few years ago it was exceptional for a neurologist even with a large experience to see a case of typical narcolepsy. I have been impressed by the fact that at least three cases have come under my observation within a year." Were one to argue from these considerations a case might be made out for an actual increase in disordered conditions of sleep somehow related to the times in which we are living, and their ascription to processes arising out of epidemic encephalitis might be plausibly offered as one explanation, but at present I am far indeed from being convinced of any frequent ætiological association of the latter with

the former. Whether any apparent increase can be accounted for, to some extent, by augmented attention on the part of clinicians is a speculation not easily to be substantiated one way or the other; and as for the actual question of numbers of cases it also cannot be decided in any positive sense.

At the outset it appears desirable to discuss certain principles of a general kind which are highly important for the understanding of sleep problems.

NOSOLOGY.

From the viewpoint of nosology it is unscientific and reactionary to allude to any of the disorders of sleep as *diseases*. In particular, to describe the variety called narcolepsy as a *morbis sui generis* is a nosological error, yet in the communications of Henneberg [36], Redlich [70], Adie [1] and others this regrettably occurs *passim*. That a special *clinical* type of sleep disorder, a clinical syndrome corresponding to Gelineau's [28] original description of a "neurosis" to which he gave the name "narcolepsy" exists, may or may not be regarded as established; but, at the most, it remains only a clinical combination. The problem here is precisely analogous to that of epilepsy; which cannot be accounted a disease *per se*; fifty years ago Hughlings Jackson was pleading for recognition of "the epilepsies" as physiological, not pathological, conditions; epilepsy is a mere symptom, and idiopathic epilepsy is epilepsy of as yet unknown origin. Similarly, the morbid or diseased conditions of which narcolepsy is nothing else than the clinical manifestation still escape us in some cases, no doubt, but there can be no narcolepsy of any kind without a cause. No one has put the matter more clearly than Lhermitte [45], as the following citation shows: "Admettre la nature névrosique de la narcolepsie, c'est admettre par le fait même qu'elle est une maladie au vrai sens du mot, c'est-à-dire un état pathologique lié à la même cause et ressortissant à la même thérapeutique. L'énoncé même des caractères essentiels d'une 'maladie' suffit à montrer que la narcolepsie ne peut à aucun titre être assimilée à une affection autonome." And even if we take the particular syndrome of narcolepsy in the sense understood by Gelineau we shall see that recently more than one case has been reported in which it has appeared as a sequel to an attack of epidemic encephalitis, rendering its isolation as a *morbis sui generis* more impracticable even than before.

TERMINOLOGY.

As already remarked, the term "narcolepsy" has been employed for more than forty years (Gélineau's paper having been published in 1880) in the vaguest way to signify any clinical variety of paroxysmal diurnal sleep, in recurring attacks of variable duration, or, indeed, of prolonged sleep states, the association of which with such known conditions as hysteria or other psychoneurosis or psychosis is unmistakable. Let it be noted that Gélineau's [28] definition—"Une névrose rare, caractérisée par un besoin subit, irrésistible, de dormir, ordinairement de courte durée, se produisant à des intervalles plus ou moins rapprochés et obligeant le sujet à tomber ou à s'étendre pour lui obéir"—is not of itself calculated to delimit the conception, as some recent authors have assumed, hence the vicissitudes which that conception has undergone, and which justified Lhermitte amply in alluding to "the narcolepsies," an expression which I myself consider eminently reasonable. Gowers [32] was one of the first to desiderate restriction of the expression, though recent writers have neglected his work; he pointed out that cases of *continuous* sleep should have another designation, as also those cases in which a sleep state is interrupted only when the sufferer is roused, for which he rather favoured the discarded term "somnosis." His conclusion was that narcolepsy should be used solely for cases in which "definite brief sleep interrupts a normal state." Naturally enough, it is impossible to say where the precise line is to be drawn between short and prolonged sleep (useful though the distinction is), and, for that matter, between sleep and lethargy, or trance; a recurrent tendency often characterizes trance-like states, while the question of whether the patient wakes spontaneously or only if roused cannot be utilized as a diagnostic criterion, since both conditions are frequently seen in one and the same case at different times. The truth is that all these distinctions are highly artificial, a consideration stressed recently also by Worster-Drought [96], who follows others in using the term solely in a symptomatic sense, to include all states of recurring diurnal sleep, whatever the ætiology.

A tendency, however, has revealed itself since the publication of Loewenfeld's [47] paper on the subject in 1902 to regard the narcolepsy of Gélineau as a special form constituted by a double symptomatology, viz., the combination of attacks of sleep with a peculiar proneness to the development of a transient condition of physical powerlessness under the influence of emotion, so that the patient's knees give way and he

may sink to the ground, without any loss of consciousness ("cataplexy"). This interesting phenomenon was noted by Gélinau's patient to occur when he laughed heartily, was observed also in Loewenfeld's case, and was raised by the latter author to the level of a diagnostic feature of narcolepsy *sensu strictiori*. Following him, Henneberg [36], Redlich [68], Stocker [88], Kahler [42], Jolly [41], Singer [77], Münzer [59], and some other German authors consider the combination pathognomonic of narcolepsy, and would reserve the use of the term for such cases only, a line which is also strongly advocated by Adie [1] in his recent able thesis on the subject. On the other hand, Goldflam [30], Curschmann and Prange [15], and others hesitate to regard attacks of powerlessness as essential to the conception; Matzdorf [52] is convinced of the occurrence of rudimentary and atypical cases which do not correspond *in toto* to the above-mentioned combined form, and in this respect is followed by Stiefler [87] in his latest paper. Along with a typical case two others characterized only by sleep attacks are included by Janzen [40] under the same designation, while a similar attitude is adopted by Adie, who accepts a case of his own, and two reported by Goldflam, in which no powerless phenomena were observed, as belonging to "true narcolepsy," and says in so many words that "sleep attacks alone may occur in genuine cases."

Experience should surely have convinced the neurologist that no good purpose is served by a hard-and-fast schematization of a clinical syndrome—which is all that narcolepsy can possibly be—to fit a conception based solely on an original description; as we have just seen, some previous writers are compelled to widen the horizon of Gélinau's narcolepsy, a procedure which in my opinion is desirable and inevitable. The four personal cases detailed below belong clearly to the combined category of sleep plus emotional ("cataplectic") attacks, but my contention is that this category is nothing else than a special variety of narcolepsy, and that the latter expression, if it is to be employed at all, can have nothing else than a purely symptomatic and non-committal significance, and under no circumstances can be used for a "disease."

This consideration leads to a further point in terminology. "The Greek word *νάρκη* signifies, according to Liddell and Scott, "numbness, deadness (Lat., torpor), caused by palsy, frost, fright, &c.," whereas the characteristic of the clinical states that here concern us is their *apparent* resemblance to natural sleep. Hence some think a preferable term is "hypnolepsy"—an "attack of sleep"—and it is interesting to note that this suggestion had already been made, not

originally by Singer [77] (as he, in ignorance of previous work, appears to think), but by Foot [25], and that as long ago as 1886. It was also advocated by Carl Camp [9] twenty years ago (1907). But "narcolepsy" has been given so long a start that it will perhaps now scarcely be overtaken.

The most recent terminological suggestions come from Wenderowicz [92], who proposes "hypnolepsia genuina" for the Gelineau combined type, "hypnolepsia symptomatica" for the same type appearing as a sequel to, or in association with, a known pathological condition, and "narcolepsia" for symptomatic hypnoid conditions arising in the course of various diseases. I do not feel inclined to adopt this rather elaborate and unnecessarily dichotomizing classification, and conclude by repeating that for the purposes of this communication "the narcolepsies" stand for hypersomnic varieties of sleep disorder, whatever their ætiology; among which it is convenient to distinguish a combined type corresponding to that so well differentiated by Gelineau.

PERSONAL CASES.

Case 1.—Male case. Duration, three years. Cause unknown. Typical diurnal seizures of "natural" sleep of brief period, associated with typical attacks of tonelessness in limbs under the influence of emotion. Additional symptom, frequent attacks of diplopia.

P. O. R., aged 24. Occupation, railway carpenter; unmarried.

History of present illness.—In April, 1924, the patient had his first attack of irresistible sleep when actually on the top of a signal post executing a repair. He managed to climb down and fell fast asleep at the foot of it, for perhaps half an hour. Ever since, he has suffered from continually recurring diurnal attacks of sleep, not a single day passing without them. About the same time as the original attack, or rather later, he noticed occasional double vision, independent of the sleep "turns," the images being on the same horizontal level and a little way apart. At a period subsequent to April, 1924, but not determined with exactitude, he noticed that whenever he laughed heartily he suddenly experienced a giving way of the knees, so much so that on several occasions he sank to the ground powerless, but was up again a few seconds later. Apart from this triad of symptoms he has no other complaint whatever. He has continued at his work.

Previous history.—Two years previously, playing football, he met with an accident and was badly concussed, but the skull was not fractured. Venereal disease has never been contracted.

Family history.—Nil ad rem.

Condition on examination.—The nervous system is normal in all respects, no trace of any organic condition being discoverable. There is no ocular paresis. Optic discs clear. Reflexes normal. The patient has not put on weight, weighing at present 12 st 4 lb., the same as at the outset. His facies reveals a state of mind of some anxiety in respect of emotional influences; rather frowning and somewhat subdued, he preserves a forced gravity. "I don't laugh any more than I can help" (see fig. 1).

Wassermann test in the serum, negative. X-ray picture of the sella turcica and vicinity, normal. Blood-sugar estimation (Dr. O'Flynn), normal curve.



FIG. 1.—Facies. Case 1.

This case conforms entirely to the syndrome of the first division of the first group (see below), presenting the combination of attacks of sleep and of "cataplexy." The former are always of brief duration, rarely exceeding ten minutes. From them the patient either awakes spontaneously, or can be at once aroused by a touch; he immediately feels fresh and continues his job. There is no background of continuous sleepiness, and no conscious feeling of physical tiredness or fatigue. The patient has slept many times while waiting his turn to come into my out-patient clinic, yet he never sleeps once he has entered, however long the examination. Personal observation of the sleep shows it to be seemingly a state of natural slumber, with no abnormal manifestation. At night, he passes some eight hours normally in sleep and has no

difficulty in awaking. In regard to the "powerless" phenomena, the sole excitant appears to be laughing, no other modality of emotional stimulus precipitating them.

Case 2.—Male case. Duration, nineteen months. Cause unknown. A brother suffers from some variety of so-called epilepsy. Typical diurnal attacks of sleep, and numerous attacks of cataplexy, especially with laughing but also under the influence of other emotions. If the patient forcibly keeps himself awake an attack of powerlessness will supervene instead of the sleep. Neurological examination during one of these reveals temporary complete loss of deep reflexes and an extensor response. Additional symptom, increase of weight, amounting to 2 st. since onset.

E. C., aged 26. Occupation, bricklayer; married.

History of present illness.—One Saturday evening, nineteen months ago, the patient was handed a paper informing him that he had won £5 in a football competition sweepstake. At this unexpected news, in the very moment of excited rejoicing, he suddenly felt helpless, his head dropped down, his limbs gave way under him and he "flopped" to the ground in a state of complete powerlessness. His head was sunk on his chest and he remained motionless, unable to move a finger, for about a minute. During the whole of the time he was entirely conscious of what was going on round about him. Immediately on recovery he felt perfectly well.

A short time afterwards (exact interval not known) he had his first attack of sleep, the circumstances of which are not remembered.

Ever since, he has had attacks both of sleep and of loss of power in the limbs under the influence of any emotion, the former occurring every day, often many times a day.

(1) *Sleep attacks.*—These are apt to occur particularly during his work, that of bricklaying. He often finds it monotonous, laying one brick after another, and the attack is usually ushered in by his mind wandering off his job: "I feel so used to it that my mind wanders off, where, I cannot tell, and then I drop off." The duration of the sleep is from three to four minutes; it is not preceded by any feeling of physical tiredness, but rather by this sort of "day-dreaming." Whenever he awakes he feels quite fresh. He either awakes spontaneously or is easily roused by a touch or a shake, but during the attacks he is soundly asleep, completely oblivious of his surroundings, and as a rule not dreaming. He has often fallen asleep at meals, "with my fork half way to my mouth." On the whole, he is as liable to fall asleep in the evenings at home as at work, yet he is confident that the warmth of the room, the time and place, make not the slightest difference, nor does the matter of interestedness arise. "I fall asleep at the pictures, or during a business conversation, just the same."

(2) *Attacks of loss of power and tone.*—The attacks of "tonelessness" arise in two distinct ways, either under the influence of emotion, or *because he is trying to avoid an oncoming sleep attack.* In regard to the first of these, any excitement suffices. Thus: "At a football match my legs give way just when some one is about to score a goal." Temper will bring on an attack, and it is particularly noteworthy that the tendency to it is always aggravated if the patient thinks that people are looking at him. "If I am playing the fool with the baby and my wife looks on and 'chips in,' I am sure to have an attack."



FIG. 2.—Facies. Case 2.

Laughing heartily never fails to bring on one of these "turns." It is equally remarkable that there is sometimes a relation between the emotion and the part of the body involved for the moment in the particular action concerned. Thus: "If I go to throw a stone at a glass bottle and any of the fellows are looking, the power seems to go out of my arm." "If I go to shoot the ball at goal and I see the fellows watching me the use goes right out of my leg; I simply can't do it."

According to the patient's own description, in these seizures the head falls forward on the chest in a nodding movement, the limbs are absolutely useless and powerless, the whole thing lasts a minute or two, and immediately after he is "as right as rain" and has no desire to sleep for the next hour.

As for the second causation, he has for long observed that *if he endeavours to keep himself awake forcibly, when sleep is imminent, an attack of powerless-*

ness will supervene, unaccompanied by any conscious emotion (unless we are to assume that the effort to avoid sleep is itself coloured with emotional tone). In the event, one or other attack is certain, though there have been occasions when deliberate shrugging of the shoulders has seemed to prevent it.

Of the greatest interest is the fact that when he has been asleep and dreaming, *the emotional content of the dream has precipitated an attack of powerlessness*. The worst he has ever experienced lasted for about a quarter of an hour, and occurred under the following circumstances. He had fallen asleep and was dreaming of a murder. The emotion experienced in association therewith brought on one of the "loss of power" attacks, so that he at once awoke and was fully conscious but was utterly unable to move a single finger. He thought he heard his brother and sister coming up the stairs; he tried to call to them but could not make a single sound; the more he tried the more intense became his emotion and the more absolute his helplessness; he lay thus, flat on the floor, motionless but suffering acute mental distress, for some fifteen minutes ere the attack dissolved itself spontaneously. Similar but less severe attacks have occurred when he has been dreaming of "terrible happenings" on other occasions.

Ordinarily, the patient's night sleep is of normal duration, and he wakes readily enough in the mornings.

At the commencement of his illness—which has never interfered with his daily work—he weighed 10 st. 6 lb.; he now weighs 13 st. (see fig. 2).

Previous history.—He has had no previous illness of any import, and no head injury.

Family history.—An elder brother, aged 32, suffers from some kind of fits. These began in 1919 and he has had only three in all. From the description given it is difficult to determine their exact nature; it appears he falls unconscious and is stiff in his limbs, but there is no change of colour, tongue biting, or involuntary micturition. As he served in the army during the war and saw much fighting, it is possible they have a psychogenic basis. Otherwise, the family history is negative.

Condition on examination.—The nervous system is normal in all respects. The reflexes are entirely normal, both cutaneous and deep. There is no ocular defect; the discs are clear. Wassermann reaction in the serum, negative. X-ray examination of the sella turcica shows it to be if anything on the small side. Blood sugar curve (Dr. Lawrence), normal in character.

The clinical value of this striking case of combined narcoleptic and emotional attacks is enhanced by the fact that I was able to observe one of the latter from beginning to end and to examine the patient's neurological condition during it. Dr. MacDonald Critchley, the present Registrar at the National Hospital, was with me at the time and helped materially in the examination, which was of necessity hurried.

Description of attack of "powerlessness."—While I was occupied

with another patient, E. C. was sitting behind me and, as afterwards appeared, was endeavouring to keep himself from falling asleep. Suddenly I heard a slight groaning sound coming from him, and at once looking round I saw his head nodding gently on his chest as he sank forward into a bent position and a moment or two later slid or "slithered" off the chair to the floor. The arms were by the side and the fingers semiflexed; the eyes were closed. Lifting the arms I found them absolutely atonic and flaccid; when let go they fell like lumps of lead by the side. The legs similarly were absolutely atonic, sprawling out on the floor. Lifting the eyelids I observed that the pupils reacted to light slightly but definitely, while the eyelid muscles were so toneless that little or no reflex contraction took place on my touching the cornea. Testing the knee-jerks I found them *completely abolished* on both sides. In the meantime Dr. Critchley had hurriedly taken off the patient's shoe and sock on the left side, and testing the plantar reflex obtained a slight but left definite *extensor response*, which he demonstrated to me and which I corroborated.

Just as we were finishing this rapid examination the patient suddenly said, "I'm all right, sir," in his ordinary voice, and with a faint smile. Muscular power came back; he moved his limbs, got on to the chair, and told us *he had been conscious the whole time*. He described what we had done, from lifting the eyelids to scratching the sole of the left foot. The duration of the whole attack was from sixty to ninety seconds. Testing his knee-jerks again, I found them *active*, even brisk, on both sides, two minutes after he had recovered.

So far as I am aware this is the first time a neurological examination of a patient in the cataplectic state has been recorded. When Adie's paper was published (September, 1926) it was therein specifically remarked that "no patient has been examined by a competent neurologist while in the cataplectic state."

I shall refer at a later stage to the significance of this observation, supplying as it does details of much importance for the study of the mechanisms involved and for the problem of the nature of the emotional attacks and their relation to the narcoleptic phenomena.

Case 3.—Male case. Duration, twenty years. Cause, unknown. There are three separable types of attack in this case; (1) typical short diurnal sleep seizures; (2) typical (momentary) attacks of loss of power in the limbs under the influence of any excitement, laughter or

rage; trance-like states of "absolute paralysis" during which no movement is possible, while consciousness is quite intact, brought on not by emotion but usually when patient is resting or sitting quietly, sometimes when on his feet.

T. T., aged 41. Occupation, boilerman: married.

History of present illness.—(1) As far as the patient is able to recall, he first noticed the tendency to *attacks of sleep* when he was in the Army in India, some twenty years ago. Scarcely a day has passed since then without his having fallen asleep, not once but a number of times. Without any preliminary warning in the shape of tiredness or sleepiness he suddenly falls "dead asleep"—a dreamless slumber of some four or five minutes' duration, from which he wakes spontaneously, or is aroused with ease and promptness. He has had "dozens" in the day. He has fallen asleep on his feet, and on one occasion injured himself by knocking against a lamp-post. He has had such attacks at his work, during meals, under every variety of circumstance, and cannot assign them to any special cause, such as monotony of occupation, warmth, time of year, diversion of interest, &c. As soon as the sleep is over he feels fresh and well, and makes no complaint of physical fatigue or of any general sleepiness.

(2) In addition, and for about the same period, the patient has noticed that any emotional excitement causes a peculiar sensation of weakness in the limbs, which results in their giving way, so that on numerous occasions he has sunk down on his knees, or actually fallen. For instance, on one occasion he saw a horse bolt and without further warning his knees weakened under him and he went down. Its duration is, however, exceedingly brief, "almost momentary," and yet there is time for him to be well aware of his heart "beating like anything," and of a very definite feeling of tingling over the head, cheeks, and body, "like a lot of strings moving over my face." "For the moment I feel as if my blood were clotting." Laughter brings on these attacks of loss of muscular power, as well as annoyance or anger. In his own words: "If I were to try to strike one of my children it would come straight over me before I could do so, and I would go flat on the floor." This has actually happened on more than one occasion.

(3) The third type of attack is as follows: at any time, usually when sitting quietly in a chair, lying on a sofa, leaning against a wall, and so on, there will suddenly steal over him a "paralysing feeling"; his eyes close but he never loses consciousness and is acutely aware of what is going on, his limbs relax and while the attack lasts he is *absolutely incapable of moving* a finger tip through a fraction of an inch. "I am paralysed from head to foot; some one could murder me and I could not move." On more than one occasion he has had a cigarette in his hand when this type of attack came on, and has actually burnt his fingers badly without being able to make a single movement to let it drop. The patient says that he "fights against it" inwardly by every means he can think of, yet not a sign of this is visible to the looker-on, who sees him

lying or sitting motionless. It appears that he eventually is able to make a grunting noise in his throat to attract the attention of his wife or other person; if he is touched or shaken forcibly the spell is at once broken and he recovers instantaneously. During the attack he is unaware of any feeling of fear, though he can neither move nor speak, but he is frequently conscious of his heart beating, "as if it were bursting." The duration of the attack is usually from three to five minutes.

He made spontaneously the interesting statement that "if I was to try and prevent myself from a sleeping attack one of my paralysing attacks would come on."



FIG. 3.—Facies. Case 3.

The patient's ailment has never prevented him from continuing at his work, and he does not complain of anything else than the symptoms described above. For years he has given up all thought of amelioration, having consulted many doctors and visited various hospitals without avail.

Previous history.—Rheumatic fever at the age of 9. Extremely moderate in alcohol. Venereal disease denied. No accidents.

Family history.—One of his five children died with rheumatic fever. Otherwise, negative.

Condition on examination.—The nervous system is normal in all respects. Optic discs normal. Ocular movements normal. Reflexes all normal. Has

not put on weight to any extent (see fig. 3). X-ray of sellar region shows it to be normal. Wassermann test in the serum, negative. Heart normal. Blood-pressure, 135 mm. Blood-sugar normal, and complete urin-analysis also (Dr. Lawrence).

This third personal case similarly conforms to the group of combined narcoleptic and tonelessness attacks, and is of especial value, in that it furnishes evidence of the occurrence of trance-like states independent of emotional excitation. It also is of peculiar interest owing to the transition from sleep attacks to "paralysing" attacks if the former are forcibly checked. When Cases 2 and 3 are compared it will be realized at once that between them they supply clinical data which throw light on the possible interrelation of the sleep and the emotional syndrome. To these matters we shall return immediately.

Case 4.—Male case. Duration, two years. Cause, indefinite illness two or three months before, diagnosed as epidemic encephalitis. Typical short diurnal attacks of sleep, with attacks also of loss of power in the limbs (often local) under the influence of emotional stimuli.

A. B. C. D., aged 18. Schoolboy.

History of present illness.—Nearly two and a half years ago the patient, when at school, suffered from some kind of febrile ailment, thought at first to be influenza but later asserted to have been epidemic encephalitis. No diplopia was complained of, nor was abnormal sleepiness or sleeplessness a symptom. Within a period of not more than a month or two, however, he put on no less than a stone and a half in weight, and at the same time began to have sudden attacks of "sleep" at meals, or when unoccupied or uninterested. An imperious desire to close the eyes was the aura, and immediately they closed he fell asleep. The duration was usually extremely brief, amounting merely to half a minute or even less, but on occasion it extended to a quarter of an hour. They have continued without intermission ever since, recurring several, sometimes many, times a day. In these attacks the patient is not as a fact deeply asleep; on the contrary, he is immediately aware when he is touched, when he is spoken to, when anything goes on round him; on a number of occasions he declares he has not been asleep at all, but has presented merely the appearance of sleep, for his state he thinks is more akin to that of "day-dreaming," a sort of "reverie" which is different from ordinary sleep. Once in a railway train the desire to close the eyes overmastered him, and instantaneously a book he was holding fell heavily from his hands; the abruptness of the onset of the sleep attacks always strikes him as peculiar. Night sleep is normal and of normal duration.

From the commencement of the affection another, to him very curious, symptom has manifested itself. It showed itself first on the occasion of a

school steeplechase. He had to jump a hedge, and as he approached it running he suddenly felt a momentary anxiety whether he could do it or not. On the instant his limbs relaxed and he fell helpless against the hedge, completely unable to get his legs to answer his call for an effort. Within half a minute he had recovered and surmounted the obstacle without difficulty. On many occasions since, a similar but very brief failure of power has made its appearance, notably when he is playing tennis. Just as he is about to serve the ball a thought flashes through the mind that he cannot do it and an equally momentary weakness of the right arm develops; by an effort he overcomes the loss of power and delivers his service usually so well that the momentary hesitation is scarcely observed.

The toneless or powerless attacks are thus largely local and of extreme brevity, but it is otherwise with the act of laughter. He has cultivated what he calls an "artificial" or "unnatural" laugh, because on one occasion when laughing heartily he became alarmed at a sudden weakness in both his legs, so that he nearly fell to the ground. As there were onlookers he felt highly sensitive about it; he now avoids the possibility of a recurrence by laughing in an unnatural way, "outwardly" and not "inwardly." He has some difficulty in describing exactly what he does at such times, but it is sufficient to prevent the development of the phenomenon of temporary weakness.

Previous history.—With the exception of the illness already alluded to the previous history is negative, and there is no record of head injury.

Family history.—On both sides of the family cases of "bad temper" in an aggravated form have occurred. His mother is an "exceptionally nervous woman."

Condition on examination.—A bright and highly intelligent boy, with a fine scholastic record, he shows no sign of any organic affection of the nervous system. All the usual methods of examination have proved consistently negative.

The clinical interest of Case 4 resides mainly in the inapplicability of the term sleep to the first kind of seizures, which more closely resemble reveries (though outwardly they are like the sleep state); in their absolute suddenness and brief duration; and further, in the almost larval or embryonic type of the cataplectic attacks, which are often scarcely more than momentary and may well pass unobserved; in their frequent restriction of range, and in the apparent success with which the patient manages to prevent them from reaching fuller development.

CLASSIFICATION.

In the present state of knowledge a complete ætiological or pathological classification is out of the question. We are compelled to fall back on an empirical clinical grouping. In my opinion a distinction into "idiopathic" and "symptomatic" varieties is not

calculated to further knowledge, for the very good reason that idiopathic narcolepsy cannot be causeless, and examples analogous to it in every respect have been seen to follow an attack of epidemic encephalitis. All narcolepsy is as a fact symptomatic, but at present we do not always know of what pathological or physiological condition it is thus symptomatic. In this, as in every scientific classification, the six-century-old aphorism known as Ockham's razor ought never to be allowed to slip from the mind: "*Entia non sunt multiplicanda praeter necessitatem.*"

A purely tentative division along the following lines, however artificial, may prove clinically convenient.

(1) Recurring diurnal attacks of sleep: (a) associated with attacks of "tonelessness"; (b) without "toneless" attacks.

(2) Sleep attacks of prolonged duration, day and night sleeps running into each other; continuous sleep.

For various clinical examples of these hypersomnic conditions a pathological basis has been found, and this aspect of our subject will be examined in due course, but it has not yet been discovered for all. Further, the range of the pathological substratum is so extensive, covering cerebral tumours on the one hand, and psychopathological states on the other, that a classification founded on it would not provide any clearer idea of the essence of the disorders.

Taking the above empirical grouping, we may consider it in detail.

CLINICAL VARIETIES.

I.—Cases which definitely belong to the first subdivision of the first class (sleep attacks with attacks of "tonelessness") must still be regarded as relatively and absolutely rare. In his monograph Adie has given a précis of those (in males) reported by Gélineau [28], Henneberg [36], Goldflam [30], Redlich [70], Jolly [41], K. Mendel [54], Noack [62], Somer (2) [79], Loewenfeld [47], Stiefler (1919) [85], Stöcker [88] (his Case 4), and Singer [77], and has added one male case of his own—a total of 14, to which he appends three personal female cases—17 in all. Typical cases (in males) published before his own communication, but not included by him, are those of Curschmann and Prange [15] (their Case 2), Westphal [93], Carl Camp [9], Redlich (2) [69], Wenderowicz [92], Matzdorff [52], and Bruno Fischer [23]—8 more; since his paper appeared there have been added those of Janzen [40] (his Case 2), Hilpert [37], Spiller (3) [82], and the first three here supplied by myself—a total of 30 male cases. In respect of this first

variety of narcolepsy in the female sex, Adie says that "hitherto the only published female cases were two described by Nevermann and by Kollewijn of "narcolepsy in pregnancy," but while these are judged by him not to have been cases of "true narcolepsy," "for sleep attacks alone occurred and they ceased after delivery," he has overlooked those recorded by Kahler [42], and by Guleke [35], both of which are highly characteristic, as well as the female cases of Gowers [33], and others (see below). Recently a typical case in a woman who subsequently developed disseminated sclerosis has been briefly recorded by Jacobsohn [39]. This gives us 6 cases in the female sex, to set against 30 male, a proportion of exactly 5 to 1 in favour of the latter.

There fall also to be included in this same clinical group those which have seemed to be consecutive to an attack of epidemic encephalitis, viz., the cases of Stiefler [86] (1924), Missriegler [55] (this case, of much interest, has been seemingly overlooked by both German and English workers), Adie, Münzer [59], Symonds [89], Stiefler [87] (1926) (his Case 2) and my fourth case, seven in all, and all males. This raises the sex ratio to over 6 to 1.

In every one of these forty-three male and female cases (I do not doubt that I may have overlooked some others unintentionally), the clinical record specifically states that in addition to recurrent diurnal attacks of paroxysmal sleep, the individual concerned exhibited in greater or less degree the phenomenon of loss of tone in the skeletal muscles (in one or other part), under the influence of stimuli of the emotional series.

II.—Taking next the second subdivision of the first class (and here I shall include both those cases in which the "toneless" attack has been looked for but not found, and those in which no reference is made to it), we find numerous instances in both old and recent literature. The recent cases are those of Adie [1], Redlich (his Case 3) [69], Goldflam (2) [30], Curschmann and Prange (their Case 1) [15], Janzen (his Cases 1 and 3) [40]; and, among the older ones, after having read through all the original records, I shall include those reported by Chavigny [13], Foot [25], Morton [58], Caton [12], Ewen [21], Pitres and Brandeis [66], and Rybakoff [74]—all in males. The female cases of this subdivision comprise those of Gowers [33], Blodgett [4], MacCormac [50], and possibly that of F. Fischer [24]. In all of these, male and female, no cause for the narcoleptic manifestations was discoverable. But when we come to similar cases in which an association with a definite pathological state seems established,

the numbers increase materially. Of the postencephalitic cases we may enumerate those of Stiefler [87] (his Case 1), Perrier (2) [64], Wenderowicz [92] (his Case 2), and Redlich (this case appears to me uncertain); typical cases developing on a basis of *commotio cerebialis* have been published by Lhermitte [46]; others as clearly linked to one or other variety of epilepsy are those of Féré [22], Gowers [32], Worster-Drought [96], Goldflam [30] (his Case 5), Brailovsky [5] (some others here are omitted as being rather indefinite); cases arising on a hysterical or other psychopathological basis have been reported by Camuset [10], Ballet [2], Laehr [43], McCarthy [49], Naimiack [61], Carlill [11], Myers [60], Worster-Drought [96], Brailovsky [5], and many more; a syphilitic infection was thought to be responsible in one of Lamacq's [44] cases. It would be easy, indeed, to enlarge still further this class of recurrent diurnal narcolepsy of comparatively brief duration, for I have made no reference to arteriopathic hypersomnia, or to the sleep attacks of certain forms of drug-taking, or of certain cases of cerebral tumour. Most of the cases of the latter two categories, however, come in reality under our second clinical division. What impresses the student when he surveys this large class is, that as far as recurring attacks of irresistible diurnal sleep are concerned, there is no affinity whatever between them and any one, specific, invariable form of disease.

Seeing that brief attacks of diurnal sleep can and do occur as a monosymptomatic variety of narcolepsy, it becomes a question of considerable interest whether the *Tonusverlust* that develops on the heels of strong emotion may not also be found monosymptomatically; if so, what place is it to be assigned in the narcoleptic category? As far as I can ascertain from a complete survey of the literature, no case of attacks of loss of power or tone through the influence of emotion, occurring by themselves, is on record.¹ But attention may be directed to the following clinical data:—

(1) In Somer's second case, that of a youth of 20, the "toneless" seizures took place not only under the influence of emotion but also after the patient had been walking or standing for a while, being then unaccompanied by any obvious affective experience; further, they were noticeably more prominent in the picture than the attacks of sleep, which by comparison were few and far between.

¹ Since this paper was written a case of cataplexy has been published by R. D. Gillespie (*Journ. of Neurol. and Psychopath.*, July, 1927) in which "affective attacks" occurred practically alone. Yet sleep apparently of abnormal quality was an occasional afternoon occurrence.

(2) In Symonds' post-encephalitic case the two types of attack occurred at different periods, for when the patient came under observation he was suffering only from the affective seizures, the sleep seizures having ceased and being replaced by insomnia. Conversely, the illness in Hilpert's case commenced with the development of affective attacks, which eventually disappeared, although the sleep attacks continued.

(3) Berliner, Hoff and Schilder [3] have recently described a case of monosymptomatic *Tonusverlust*, which they reckon "in die nächste Nahe zum Tonusverlust des Einschlafens und damit zum Tonusverlust der Narkolepsie." The attacks in this case (an organic one) appear to present an intimate similarity to those of the narcolepsy group, but sleep attacks did not occur.

Clearly the effort to circumscribe the conception of narcolepsy alluded to above becomes more dubious than ever if cataplectic seizures can appear by themselves, or be a feature of other states than narcolepsy proper. Further, in this same connection, the importance of *larval or incomplete varieties of narcolepsy* must be underlined. The following personal case, recently observed, seems to me particularly illuminating.

Case 5.—Male case; larval or incomplete variety. Duration, three years. Cause unknown.

H. G. B., aged 32. Occupation, business.

History of present illness.—For about three years the patient has noticed the occurrence of peculiar attacks, of brief duration, during which he seems to be unable to move his eyes; he finds himself staring at some object, and in a kind of day-dream; the object then becomes indistinct, as if seen through a haze, and only by a strenuous effort can he cut short this state and break into its fixity. If no effort is made the phenomenon disappears spontaneously within a minute or two. He has also observed that on occasion this immobility seems to spread so as to involve other musculatures, giving him the feeling that he is quite unable to move any part of his body, yet at the same time the thought comes into his mind, "Oh yes, I can move if I like"; as a fact, however, he always remains motionless for an appreciable period, measurable in seconds. No emotion of any conscious kind initiates these spells.

For about the same time (three years) he has repeatedly noticed that under the influence of any excitement or other emotional stimulus he turns deathly pale and loses control over his limbs; in his own graphic language, "I feel as if I had no knees"; when playing a game at bridge, wondering what sort of a hand he is going to pick up, he feels his legs "disappearing" and is thankful he is sitting on a chair. With some five or six friends he meets regularly at a

restaurant for coffee, and the decision as to who pays is reached by one of the circle piercing the menu card with a pin haphazardly; the letter nearest the pinhole is taken, and the letter of the respective surnames of the members nearest that in alphabetical order decides. During this trifling procedure he has frequently turned "as pale as a sheet" and, standing on one occasion, had to hold on to the furniture as his lower limbs were sinking. His friends have noticed his demeanour and uncharitably attributed it to unwillingness to pay, whereas in fact it has been the outcome of the affective experience. Hearty laughter produces the same result.

On no occasion, as far as can be ascertained, has the patient had sleep attacks, yet many times during the day he suddenly becomes conscious of "a warm feeling round his eyes," leading him to close them for a moment, and he remarked spontaneously that he always feels that if he chose to he could then allow himself to sleep. As a fact, he has never thus succumbed to the impulse.

Family and previous history.—Negative

Condition on examination.—A normal finding in all respects.

Had our knowledge of narcoleptic syndromes not widened in recent years I doubt whether the real nature of this case would not have escaped me; as it is, I confidently assign it to an abortive or incomplete class in the general group, at the same time stressing the point that *only the affective or "Tonusverlust" attacks have passed into a characteristic stage*. And it is a further matter of no little interest that this patient also exhibits almost a cataleptic immobility (cf. my Case 3 above) which, brief or momentary as it is, is apparently independent of emotional excitation.

III—If we take, next, sleep seizures of a prolonged or continuous kind, we are familiar with their occurrence under equally variable pathological circumstances. Clinical distinction here between natural sleep and states of stupor (anergic, catatonic) or of semi-coma is often enough difficult to establish, and the same is true of cataleptic or trance-like conditions and of those associated with drug addiction. Prolonged hysterical sleep is well known and has been the subject of numerous communications (e.g. Ræcke [67]); in this connection no recent writer has mentioned the case of the "sleeper of Oknò," as narrated by Froderström [27], who slept for thirty-two years. The curious will find in the volume by Gould and Pyle [31] valuable historical references to cases of protracted sleep of the hysterical, cataleptic, and stuporous kind. Similar more or less continuous sleep states also accompany some cases of such organic intracranial conditions as cerebral tumour or abscess; they have been known for many years, and have been made the subject of numerous useful studies (Righetti [72], Franceschi [26], Soca [78], Purves Stewart [83];

more recent communications are those of Bychowsky [8], Pette [65], Lucksch [48]; Thomas, Jumentié and Chausseblanche [90]; Souques, Baruk and Bertrand [81]).

Finally, I need here only mention the well-known short or, much more commonly, protracted sleeping states of epidemic encephalitis and of trypanosomiasis to complete the catalogue of the narcoleptic syndromes belonging to the second clinical group.

CLINICAL SYMPTOMS.

(I) *Sleep.*

Although the term sleep is freely applied to the phenomena of the great majority of the cases usually classed as of narcoleptic character, the ostensible reasons for this require to be examined. It must be apparent to any critical mind that no definite clinical distinction can be drawn between degrees of sleep, which range from merely "dozing" with the eyes shut, on the one hand, to a profundity of unconsciousness not easily to be separated from a comatose state, on the other. In clinical practice distinctions and contrasts are far less easy to draw than they are on paper. Can sleep as a fact be readily differentiated from sleep-like states, and if not, where are the latter to be considered as beginning or ending? In the direction of deepening unconsciousness one passes by easy gradations from somnolence to sopor, sopor to stupor, and stupor to coma, as Monakow [57] long ago emphasized; but if the sleep of narcolepsy is thought to be distinguished by the fact that the patient is easily roused therefrom this is in the first place *not* true for every case, and in the second characterizes some other unconscious states not of the same nature, e.g., some forms of hysterical fit. Glancing through German literature one finds such terms as *Schlaflosigkeit*, *Schlafsucht*, *Einschlafsucht*, *Somnolenz*, *schlafähnlicher Zustand*, *Schlafanfälle*, *Torpor*, *Lethargie*, *Sopor*, in frequent use, without their apparently corresponding to any clear-cut distinctions of a clinical character. If, again, we take the descriptions of cases confidently assigned to the group of narcolepsy it is at once evident that in quite a number of instances the attack of sleep does *not* correspond to ordinary conceptions of that state, for we note that frequently the patient is declared to "have heard what was being said," or "to have been aware of what was going on round about him" (Goldflam, Westphal, Redlich [68], Somer, Chavigny, Mendel [54], and others). Even a normally light sleeper is not in point of fact asleep if he is cognizant of

what is going on. It thus becomes more than doubtful whether the sleep of the narcoleptic is to be likened in all respects to normal, healthy sleep.

Equally remarkable, and somewhat disturbing to any view of narcolepsy as just an exaggeration of a normal cycle of sleeping, is the significant observation made by not a few that the patients declare they exhibit only the appearance of sleep; they are in reality aware of their surroundings *but not able to move a single muscle or articulate a single word* (Redlich [69], Guleké [35], Bruno Fischer [23], Loewenfeld [47], and others). That is to say, the condition bears only an apparent resemblance to sleep and turns out to be transitional to the cataleptic class of seizure. In my Case 2 the attack of tonelessness looked rather like sleep, inasmuch as the patient's eyes were closed and his head nodded on his breast, whereas as a fact he was entirely conscious and awake, and the physiological phenomena were of a peculiar kind. Again, in my Cases 3 and 5 trance-like states occurred, apart from emotional excitation, which bore the external marks of sleep, but their content was altogether different, seeing that in point of fact the patient was fully conscious of his surroundings but unable to move a muscle. The "sleeping" and the "toneless" attacks are evidently linked to each other, in many cases, much more intimately than appears from a casual survey. Thus this interesting condition, found in many cases of narcolepsy, widens the conception and approximates it to that of cataleptic and trance-like states, to which some erroneously think it is altogether foreign. This aspect of the problem is of considerable significance.

Another argument can reasonably be advanced against the hypothesis that the sleep of narcolepsy is ordinary sleep, pure and simple. The normal subject falls asleep because he is sleepy, whereas the great majority of narcoleptics are not conscious of undue sleepiness as a prelude to the attack of sleep; nor, for that matter, curtailed as the duration of the sleep nearly always is, are they sleepy or drowsy thereafter; on the contrary, most of them say they are at once quite fresh. And again, the vast majority enjoy sleep of normal duration at night, and never oversleep themselves. It is obvious, in short, that the abnormal slumbers of the day differ from nocturnal sleep in several respects, the possible significance of which it would be well not to underestimate. Suddenness of onset of the diurnal sleep has characterized very many cases; two of my patients have repeatedly fallen asleep at meals, with their food halfway to their mouth. A quite

forgotten case reported more than seventy years ago by Graves [34] is that of a gentleman who had sudden attacks of unconquerable sleep; at meals he broke one wine glass after another by falling asleep after the act of filling the glass and during the time he was raising it to his mouth—a literal slip 'twixt the cup and the lip. This abruptness of onset is highly characteristic. There are but few exceptions to the generalizations just mentioned. Persistent sleepiness is distinctly rare, as is physical tiredness. Stiefler's [85] patient (1918) would fall asleep after the Sunday midday meal and remain in unbroken sleep till the next day; he was nearly always tired and sleepy, but was definitely alcoholic, and there was a family history of alcoholism in father, mother, and three brothers. Caton's [12] patient had a constant sleepy look and could only keep himself awake by active exercise or mental stimuli. Tiredness preceded the attacks of sleep in the cases of K. Mendel, Goldflam, Jolly, and some others. In a few cases the conditions and circumstances tending to lead to sleepiness in normal persons (monotony, warmth, post-prandial repletion) have been noticed to affect narcoleptics also, but in numerous other instances no such association has been found (cf. as an instance my Case 2; the patient fell asleep as readily during a business conversation as when at the pictures; whether he was warm or cold made no difference). Bruno Fischer's patient sometimes opened his eyes during the sleep attack, so that his friends did not always know whether he was asleep or not.

Because of these peculiarities and differences we are compelled to question any strict identification of the phenomena of so-called narcolepsy with those of normal sleep in the healthy individual, close though the superficial analogy may be, and frequently is. Had we any objective criteria to fall back on, differentiation might be more readily accomplished, but the sign of contracted pupils in sleep, relied on to some extent by Goldflam because noted by him in his cases of narcolepsy, has not a universal applicability. If the useful researches of Richter [71] on changes in the electrical resistance of the body during sleep are corroborated, it may be that along these lines light will be thrown on differences between normal sleep and certain pathological conditions nearly resembling it. He has found, for example, a gross difference in the electrical resistance of the skin in a number of patients in catatonic stupors, "some of which so closely resembled sleep that it was impossible to tell by looking at the patients that they were not asleep," as compared with the resistance during normal slumber.

Enough has been said, however, to cast doubt on all simplistic

interpretations of the diverse sleep phenomena of narcolepsy—phenomena not embodied in the terminology—and to suggest we are dealing with syndromes not consisting in recurrences of natural sleep but presenting features which offer a link of union with other psycho-pathological conditions of particular interest.

(II) *Attacks of Loss of Tone and Power.*

This feature of our first variety of narcolepsy is of consummate interest, because, or in spite, of the fact that it bristles with difficulties.

In the first place, subjective descriptions apart, clinical observation reveals modalities and divergencies of considerable importance. Perhaps the commonest type of attack is that in which, under the influence of emotional excitement, a toneless and powerless state of the skeletal musculature supervenes, with the consequence that the person concerned finds his knees giving way and he sinks to the ground; after a brief period, measurable usually in seconds, tone and power return and he is able to get up again. Attacks corresponding to this general account have been remarked in all of the forty-three, male and female cases which I have collected, but they may vary materially in degree and extent. Sometimes the patient is conscious of no more than a sinking at the knees, possibly scarcely noticeable to the onlooker; in other instances the seizure is complete, affecting neck, trunk, arms and legs and lasting for quite several minutes. In one and the same case the degree may differ at different times and under differing circumstances.

The actual clinical state is one of transient, combined diminution or loss of volitional power and of muscle tonus, and it is for practical purposes difficult to separate the two components. With complete outfall of tone some loss of power must ensue (cf. the apæsthesia experimentally produced by Mott and Sherrington), though the two need not proceed *pari passu*. In respect of the average condition in narcolepsy objective examination reveals both a loss of power, amounting to absolute immobility, and a loss of tone; the observation made by myself and described fully on a preceding page is of high significance, for it furnishes proof of tonelessness so profound as to result in temporary abolition of the deep reflexes. Numerous observations point to the occurrence of partial and segmental failure of power and tone. The incidents mentioned in my Cases 2, 3 and 4, are paralleled by analogous occurrences in the cases of Janzen (his Case 2), Wenderowic, Goldflam and others. In all of these power went out of the limb or limbs about to be innervated volitionally—a kind of motor inhibition, under the influence of excitement.

A second feature of the cataplectic attack is that in various recorded cases something more than, or different from, pure loss of tone takes place. Trembling (Westphal), movement of the head and protrusion of tongue (Noack), twitching movements of eyelids and face (Bruno Fischer), of lower jaw (Wenderowic), and other involuntary movements (Redlich [70], Carl Camp), have all been seen. The possibility, also, of *voluntary movements of correction* complicating the muscular weakness is specially mentioned by Adie. The absolute speechlessness of many cases is not encountered in all; my patient (Case 2) made a grunting noise as his head fell forward; Somer's patient muttered something unintelligible. An equally interesting observation is that of Redlich [69], who in one case noted that hearty laughing led to an attack of powerlessness which culminated in involuntary relaxation of both vesical and rectal sphincters.

One of the integral characteristics of the phenomenon is the full conservation of consciousness during its course, however much, in some cases, the appearance of the patient may belie this.

The exciting cause of the attacks is declared almost universally to reside in a stimulus of the emotional series, among which anger, annoyance, compassion, agitation of any kind, amusement or joy may be specially mentioned. The *act* of laughing provokes the attack more readily than any other cause, but we must note particularly that in this case the emotional stimulus itself, unless it manifests itself in laughter, does not suffice; in other words, while anger, and excitement generally, will precipitate the attack in spite of the patient's efforts to frustrate it, a stimulus arousing laughter will not produce the attack should he be able to inhibit the motor act of laughing. A consideration of the clinical data undoubtedly bears this contention out. In a number of cases it is expressly stated that only irresistible laughter culminates in the loss of power. Only when Gelineau's patient "*riaît aux éclats*" did his limbs give way. My patient, E. C. (Case 2), smiles readily enough, and laughs softly, without experiencing the cataplectic phenomenon. Stiefler's [85] patient never developed the affective attack from laughing, but only with rage or annoyance.

Somatic accompaniments indicative of the emotional disturbance, whatever its modality, are not referred to in the literature to any extent—a curious point well worth passing notice. I can find only the briefest allusion to these. One of Redlich's [69] patients said that in the seizure he had a feeling of "losing his breath"; another said he was conscious of a "warmth spreading over him." In Wenderowic's

case the patient was aware of a "pulsating noise in his head"; Somer's second patient showed pallor of the face, as does one of mine (Case 5). The case recorded by E. Mendel concerned a patient who exhibited attacks of *Tonusverlust*, during which there was pallor, the pulse was slow, and perspiration broke out at its close. My own patient, T. T., described with great clearness palpitation of the heart and a feeling of tingling over the head, cheeks and body. Doubtless somatic phenomena of these and similar kinds occur more frequently than is recorded, yet the speculation arises whether, in the case of cataplexy, the emotion does not manifest itself abnormally, to the relative exclusion of the usual outward accompaniments.

(III) *Transitions and Substitutions.*

Cursory consideration of the two types of attack might yield the impression that they consist of forms essentially dissimilar, correlated only through their occurrence in one and the same case. This is without doubt a fundamentally erroneous conception, as can at once be realized by attention to the following clinical variations.

(1) *Emotional excitement may lead not to the cataplectic but to the narcoleptic state.* This occurred with regularity in the cases reported by Kahler and Westphal. Under the influence of emotion the patient whose case is reported by Bruno Fischer felt a strong inclination to sleep. The connection is shown best of all in Gélinau's original case: "s'il a une émotion profonde, pénible ou joyeuse, le besoin de dormir est encore plus impérieux et soudain."

(2) *Sleep may be associated with or follow the cataplectic state.* During the attack of powerlessness following laughter, Matzdorff's patient felt an irresistible desire to sleep.

(3) *If sleep is prevented the cataplectic attack may ensue.* This interrelation is exhibited in perfection by my patient E. C. (Case 2 above). Similarly, in the case of T. T. (Case 3 above), interference with the impulse to sleep led to the oncoming of the "paralysing attack," to use the patient's own expression.

(4) *The cataplectic state may develop spontaneously, as does the narcoleptic attack in most cases, and be unaccompanied by emotion.* This occurred in the cases of Goldflam and of Somer (his Case 2); and in my Case 3, as we have seen, the "paralysing attack" bore no relation to emotion, as far as could be ascertained. A similar remark is applicable in respect of my Case 5.

(5) *Many, both of the sleep and the cataplectic, attacks are in reality*

identical in comprising a component which corresponds to the usual conception of catalepsy or trance. In a previous section I have furnished evidence fully bearing out this statement; awareness of surroundings, coupled with inability to move, has marked one or other type of attack in the cases of Nammack [61], Westphal [93], Somer [79], Guleke [35], Gélinau [28], K. Mendel [54], Goldflam [30], Redlich [69], Chavigny [13], Bruno Fischer [23], Loewenfeld [47], three of my five personal cases and others. The association occurs with an impressive frequency, and cannot be dismissed as accidental.

Consideration of these various divergencies must in my opinion compel us to envisage the possibility that a common factor may yet be found for all the clinical phenomena; that some not as yet clearly understood inhibitory mechanism is responsible both for the "sleeping" and for the "falling"; that the relations between narcolepsy and other clinical syndromes now to be examined are so close as to render strict delimitation of the former both impracticable and inadvisable.

RELATION OF NARCOLEPSY TO OTHER CLINICAL SYNDROMES.

(1) *Relation to myoplegia.*—As far as I have discovered, Wenderowic is the sole author who makes reference to the resemblance between the attacks of *Tonusverlust* and those of myoplegia paroxysmalis or periodic family paralysis. Yet the analogies are impressive, in spite of the considerable differences. The examination of the phenomena which occurred in the course of the cataplectic attack of my Case 2 at once suggested a certain similarity to those of myoplegia, since in their essentials they consisted of a sudden, widespread, flaccid "paralysis" of skeletal muscles with complete loss of the deep reflexes. The time was much too short for any investigation of the electrical reactions; some future observer may be able to furnish us with data in this respect. In the usual family myoplegia the attack is crescendo in character, taking, perhaps, hours to develop and hours to die away, but at its height the combination of flaccid palsy with loss of deep reflexes is identical with that reached in a few seconds in the case of catalepsy. I purposely do not emphasize these resemblances, the divergencies being obvious to everyone, yet it is well to make a note of them; according to Wenderowic a relative lymphocytosis characterizes myoplegia, and a similar blood-picture has been found in narcolepsy by Janzen and by Stiefeler [87]. The significance of this blood-change is as yet indeterminate.

(2) *Relation to catalepsy.*—This term, like too many other medical

expressions, suggests a seeming precision which, as a fact, it does not possess. By catalepsy is usually understood a state of motionlessness, of sustained immobility, with or without clouding of the sensorium; the patient exhibits the appearance of sleep, is commonly indifferent to stimuli, and often shows the phenomenon of *flexibilitas cerea* in the limbs. As a symptomatic term the word has its value, indefinite though it be; the difficulty is that both catatonia and catalepsy convey the idea of the presence of the *flexibilitas cerea* just mentioned; yet this is not a cardinal, in the sense of exclusive, feature of the condition, as I have seen it in the sleep states of epidemic encephalitis, in frontal lesions of organic character, and in other intracranial states (cf. Brissaud [6]). We need an expression to signify the condition of being "struck all of a heap," of immobility, following on affective shock, which is sometimes met by use of the phrase "catatonia attonita" (cf. *Schreckkatalepsie*). Doubtless catalepsy covers a multitude of dissimilar syndromes, but its main connotation, as given above, has received general acceptance. Many catalepsies are hysterical; the majority, indeed, are, widely speaking, psychopathological. Now we have already seen how many of the attacks of the narcoleptic are signalized precisely by this trance-like state of awareness of environment coupled with absolute inability to move a finger. No allusion is made by any modern writer on narcolepsy to the once much-discussed question of *nocturnal paresis* or *paralysis*, which formed the subject of an interesting study by Weir Mitchell [56]. While doubtless here also a number of differing clinical conditions are comprised, among them is one to which I have long given attention. I have found it in various persons, healthy and otherwise, and do not regard it as anything else than a transient physiological disorder. It consists, briefly, in a state which supervenes commonly in the morning; the subject is awake, because he is conscious and knows where he is, but for the moment he is utterly incapable of innervating a single muscle. He lies in appearance still asleep, with eyes closed, yet within is engaged in an intense struggle for movement, with which is associated an acute mental anxiety; could he but manage to move a limb through a fraction of an inch, the spell would be instantaneously broken, and with a sigh of relief he would regain full power. I have had graphic descriptions of this "sleep paralysis" from more than one patient.

Its resemblance to the "paralysing attacks" of my third narcoleptic (T. T.) is of the closest. It is a physiological catalepsy, a state of sustained immobility with sensorial awareness, and as such is of much

interest for our subject. In a large number of the recorded cases the remark is made that the patient can be roused from his narcolepsy or his trance-like condition by a touch, a shake, a movement, whereas stimuli through other sense avenues are less effective. It seems to me this observation may have possible significance.

(3) *Relation to epilepsy*.—Much controversy has raged round the question of the relation, if any, of narcolepsy to epilepsy. On the whole, most authors deny any connection between the two. Curschmann and Prange go so far as to advocate abandonment of the term narcolepsy, because "it suggests a relationship to epilepsy which does not exist." Adie repeatedly stresses the point, declaring that it is highly important "we should distinguish it [narcolepsy] from a serious disease [epilepsy] with which it has no connection whatever." A similar attitude is assumed by Kahler, Goldflam and a number more.

But there is very much to be said against differential absolutism of this kind.

(1) The immediate and obvious answer to those who object to the idea of any association between the two is, what do they mean by "epilepsy"? Unless they furnish us with a definition of epilepsy it is useless to say that narcolepsy has nothing whatever to do with it. Yet in not one of the discussions on this matter have I found the objector to give a description of what he understands by "epilepsy"; nay, further, I have noted frequently that epilepsy is still spoken of as a "disease," so little have Hughlings Jackson's doctrines made headway in this particular respect.

In my recent Harveian Lecture [94] on "The Epilepsies" (to which the reader is referred) I have advanced considerations, developed along lines suggested by Hughlings Jackson many years ago, which indicate the possibility of any motor cell-group becoming the seat of a "discharging lesion," so that an epileptic attack may take a number of seemingly very different clinical guises. The diseased condition (whatever it be) is the cause of the "epilepsy," which is a symptom pure and simple, and, as such, strictly physiological. Adopting this view of the question, I maintain strongly that *any alleged contrast between the narcolepsies and the epilepsies is merely a contrast between symptoms and leaves untouched the problem of whether or not there is a similar mechanism of production behind each*. That there may be, in point of fact, some such similarity of inhibition or release of function is surely conceivable and therefore worthy of discussion. This pathogenic aspect is dealt with later.

(2) The clinical observer must admit general resemblances between the two classes of symptom. As Hilpert [37] has recently remarked, apropos of narcolepsy: "Die Beziehungen zur Epilepsie sind demnach in jeder Hinsicht offensichtlich." It is indeed impossible to overlook the general analogies, which consist in periodical recurrence of attack, abrupt onset with or without aura, loss or diminution of consciousness, relatively brief duration; like many epileptics, many narcoleptics are fresh again soon after. The "fit" of sleep is in these respects like many "fits" of another kind. Of course the actual *content* of the "fit" is different in the two cases, but this does not affect the argument; for that matter, as I have said elsewhere, the word fit "might be legitimately employed to designate certain attacks of which motionlessness is the prominent feature." Besides, the involuntary movements of some at least of the attacks belonging to the cataplectic series offer more than just a casual resemblance to those of petit mal or of some mild epileptic seizure. Symonds observed one of these in his case, and took it to be epileptic, like petit mal; and I have already mentioned at the outset of the attack in my Case 2 the noise in the throat, the nodding forward of the head, the sinking down in a seemingly unconscious state—phenomena the analogy of which with some of those usually called epileptic it is pointless to try to controvert. If behind the ordinarily great dissimilarity of the external manifestations there is reason to postulate the action of not dissimilar mechanisms, it becomes unscientific to argue for fundamental differences between them from a nosological standpoint.

(3) Amplifying this last consideration, we may examine one or two of the arguments advanced by the supporters of the "no relation" theory. Adie says, "A most important feature of idiopathic epilepsy is that the attacks come on without apparent cause, whereas in narcolepsy the cataplectic attacks are 'reactive,' i.e., there is a definite exciting cause, namely, emotion." And again: "In genuine epilepsy the attacks are never reactive; this feature alone is sufficient to show that the two conditions are fundamentally distinct." But we have already noted that cataplectic attacks may develop spontaneously (Goldflam [30], Somer [79]), while the trance-like states of my Cases 3 and 5 also thus developed without any emotional antecedent. In the second place, the view that idiopathic epilepsy is never reactive is contradicted by familiar experience. We need not go so far as Rows and Bond [73], who explicitly affirm that "a survey of a large number of cases [of epilepsy] . . . has demonstrated that some emotional

state involving a disturbance of consciousness, and some reaction to express the emotion, have been found in every instance." But of the occurrence of what we may call reactive or psychogenic epilepsy ("affect epilepsy") most observers have had abundant proof; it is recognized by all modern writers on the subject (notably Pierce Clark), and a good illustrative example was recently published in a paper of my own [95]. This particular criterion of differentiation, therefore, does not serve the purpose.

The claim that mental deterioration and psychical defects are characteristic of epilepsy but foreign to narcolepsy must be considered of relative and not absolute value, since numerous moderate epileptics suffer from their infirmity for years without exhibiting intellectual impairment. Much depends on the severity of the case, and on the actual class of attacks.

(4) More important, as forming a positive argument, is the fact that epilepsy and narcolepsy are on occasion definitely associated. For example, one of Gowers' [32] cases was that of a girl, aged 14, with a family history of epilepsy, who had suffered for four months from attacks clearly of that nature. But she had also, during the same time, "attacks of sudden pure sleep." When bromide was given regularly the epileptic seizures ceased, but the attacks of sleep went on unchanged. Failure of anti-epileptic remedies in narcoleptic cases cannot, of course, be advanced as an argument for the essential dissimilarity of the two conditions; some epileptics do not react to anti-epileptic drugs. Since the phenomena of narcolepsy are largely akinetic we should not expect sedatives to be the appropriate treatment. Besides, there is no greater ætiological fallacy than that *naturam morborum curationes ostendunt*. A valuable case is that recorded by Worster-Drought [96], in which the patient, a man of 25, suffered from fits in childhood up to the age of 10; since 1913 three fits ("description suggesting true epilepsy") have occurred, and also numerous narcoleptic attacks of variable duration, characterized by his falling asleep "at any time, under all conditions, and often in perilous situations." Once more, one of Goldflam's [30] patients (his Case 5) suffered from narcolepsy for six years, and later developed typical epilepsy with convulsions. Other instances of the same association are specified by Brailovsky [5]* from records not accessible to me; the older cases of Féré [22] must also be alluded to in this connection, especially his Case 3, that of a youth of 21, who had both epileptic and narcoleptic seizures, the latter closely resembling normal sleep of brief duration (a quarter of an hour or less).

Féré specially noted that as the epileptic attacks increased the others diminished in frequency, and vice versa.¹

During an ordinary major epileptic attack the subject is unconscious, while motor mechanisms escape or are stimulated into abnormal activity; during many narcoleptic attacks the subject is conscious, while the activity of lower motor mechanisms is in the completest abeyance. There is here, as I consider, a certain approach to the existence of "corresponding opposites," in Jacksonian phraseology, which may yet prove to be pregnant with meaning for an understanding of their physiological counterparts. Again, during the examination of my patient E. C. (Case 2), in the course of his affective attack I was able to demonstrate the temporary occurrence of an extensor response. This is known to characterize similarly many epileptic seizures, and it has, further, been observed in normal subjects during sleep. Collier [14] found in a number of healthy children up to the age of 12, during deep sleep, a typical "infantile response" (that is, extension); directly the child awoke the normal adult plantar reflex (flexion) occurred on stimulation. It cannot be without significance for our problem that a "physiological shift," as I call it, of the same type as is seen in normal sleep and in the epileptic fit, characterizes also the cataplectic seizure of the narcoleptic.

In face of these clinical observations it would be a mistake alike to ignore the similarities and to stress the differences; the correct attitude in my opinion is to suspend judgment and to await further contributions to our knowledge. So far, however, as the preceding considerations take us, they make out a *prima facie* case for the possibility of some of the narcolepsies and of the epilepsies having a common origin.

(4) *Relation to Oppenheim's Lachschlag.*—Under the term *Lachschlag* (*Lachschwindel*, *Lachohnmacht*, geloplegia) Oppenheim [63] described two cases (one of a girl and the other of a man, aged 45), of falling to the ground under the influence of hearty laughter. From the description furnished by the relatives (for no attack was personally observed) he supposed the patient was unconscious during the few seconds only of which its duration consisted, though he says in reference to the first case, "ob volle Bewusstlosigkeit dabei eintritt, haben sie [the relatives] nicht festgestellt." Adie is inclined to look upon this *Lachschlag* as distinct from narcolepsy, whereas Jolly and Matzdorff both are impressed with the analogy it offers to the *Affektanfalle* of

¹ In a recent paper on "Epileptic Variants" (*Journ. of Neurol. and Psychopath.*, January, 1928, p. 281), I have recorded a case exemplifying a transition from epileptic to narcoleptic attacks.

the latter condition; Redlich [68] points out that the loss of consciousness in Oppenheim's cases was not absolutely certain, and mentions the cases in which sleep follows emotional excitation (see above): Goldflam, too, considers the resemblances of some significance.

I have myself observed one good case of the condition, that of a man aged 42, whose symptoms supervened on an injury to the head in the right frontal region. He noticed that when he laughed too loud he tumbled down, a condition which gradually so established itself that he had "dozens of tumbles." If he laughed slightly, he felt a sort of staggering feeling in the limbs; the louder he laughed the more he staggered; eventually he would fall to the ground, but would be on his feet again in a few seconds. Occasionally he "would go right off in the attacks," by which expression I understood from his description that he became unconscious of his surroundings for a moment or two, but not having seen the patient in such a condition I am unable to determine the exact state. By way of defence, he said to me, "I have cultivated a giggle to avoid the laugh." He had no attacks suggestive of sleep, and objective examination was negative.

The analogies which *Lachschlag* presents to the cataplectic attacks of the narcoleptic are much more impressive than the differences, so much so that it may fairly be considered a larval form of the other, or indeed, more or less identical.

ÆTIOLOGY.

The search for possible causes of narcoleptic syndromes has revealed in some instances preceding factors to which the symptoms may legitimately be attributed, but in others none of recognizable pathogenic quality has been discovered.

As regards the former, *head injury* was noted in cases reported by Kahler [42], Redlich [69], and Singer [77], and occurred also in my Case 1 above. The appearance of narcoleptic phenomena after *commotio cerebri* is mentioned by Souques [80], and has been made the subject of a careful study by Lhermitte [46]. The symptoms in the personal case of *Lachschlag* mentioned already followed an injury to the frontal region. *Alcoholism* in patient or parentage was a feature in those of Noack [62], Redlich [68], Stiefler [85], and Hilpert [37]. The possibility of an *endocrine* ætiology is suggested mainly by the interesting fact that in a considerable number of instances narcolepsy has been associated with a definite *increase in weight*, the result of the patient's becoming more fat (Hirsch [38], Ballet [2], Münzer [59], Caton [12],

Jolly [41], Stiefler [85], Lamacq [44], Redlich [69], Hilpert [37], Janzen [40], Curschmann and Prange [15], and my Case 2). The sella turcica was stated to be on the small side in those of Kahler [42], Redlich [69], Jolly [41], Singer [77] and Janzen [40]. In certain female cases the symptoms were aggravated during the catamenial flow (Fischer [24], Kahler [42]). A somewhat doubtful case reported by Dercum [17] was associated with an acromegaloid condition. We should mention, too, that a relative lymphocytosis of the blood occurred in cases published by Kahler [42], Stiefler [87], Janzen [40], and Redlich [69].

Attention must be directed also to the peculiar connection of some narcoleptic cases with *epistaxis*.

(1) The patient of K. Mendel [54] suffered from almost daily nose-bleeding between the ages of 8 and 22. When this finally ceased narcolepsy supervened.

(2) In a female case (MacNamara [51]) a girl, aged 15, had sudden attacks of profound sleep, which disappeared after a severe epistaxis, and did not return.

(3) Hilpert's [37] patient exhibited the typical combination of narcolepsy and cataplexy. An illness (? "cerebral influenza") developed intercurrently, associated with strong epistaxis, and thereafter the cataplectic attacks ceased altogether, though the narcoleptic continued.

(4) In consultation with Dr. Gordon Holmes I have recently seen a case of narcolepsy with cataplexy in a young man, with high blood pressure and slow pulse, who used formerly to have bouts of epistaxis regularly about once a month. Since the onset of the narcolepsy the epistaxis has entirely stopped.

These facts are rather striking, even though their significance at present eludes us.

Again, an origin for the narcoleptic syndrome in some disturbance of a *psychopathological*¹ kind was definitely ascertained in cases reported by Carlill [11], Myers [60], Worster-Drought [96] and Missriegler [55], and was probable in those of B. Fischer [23], Morton [58], Stocker [88] (his Case 4), and Brailovsky [5]. This aspect of the problem has undoubtedly been somewhat ignored by neurologists preoccupied with organic disease, and it might be developed further with advantage. I do not question that the so-called idiopathic

¹ Gillespie says of his case of cataplexy alluded to in the footnote on page 80, "psychological factors were evident enough, but psychotherapy had no lasting effect."

variety might be further dismembered were an adequate psychological investigation undertaken more frequently.

The data which have just been examined, together with what has been said on a previous page, apropos of clinical varieties, are sufficient to show how diverse and heterogeneous is the ætiology of the narcoleptic syndrome. To assort the causal factors is a matter of no little difficulty; a provisional arrangement might be made along the following lines:—

- (1) Traumatic group.
- (2) Psychopathological group.
- (3) Endocrine group.
- (4) Epileptic group.
- (5) Toxic-infective group (epidemic encephalitis, &c.).
- (6) Circulatory group.
- (7) Pressure group (cerebral tumours, &c.).
- (8) Group in which no *Grundkrankheit* has been discovered.

Doubtless a cross-division may occur here; again, some ætiological components are surmised rather than proved in particular cases. In others the relation of the syndrome to the apparent cause, or to an outstanding feature of the individual case with which it may be linked, remains obscure, e.g., in respect of epistaxis and diplopia. I have already alluded to the former; of the latter it may be said that it was noted in cases recorded by Janzen, Spiller, Hilpert, and myself (Case 1). Whether it is of ætiological significance is undetermined; according to Janzen it is no more than a "prehypnotic" or "hypnagogic" diplopia, occurring in many normal people if they try to resist sleep. This explanation, however, does not appear to apply to my Case 1, in which the double vision was complained of independently of the sleep attacks, yet so far I have failed to discover any objective basis for it.

For the present the student of narcoleptic symptomatology must be content to recognize the diversity of the bases on which it arises in many instances, and to acknowledge his entire ignorance of them in others.

PATHOLOGY.

No autopsy on a case of narcolepsy belonging to the first clinical division has up to the present been conducted, so far as I know. Patients do not die of narcolepsy, which, as we have seen, is no disease.

What pathological information is at our disposal is derived from cases belonging to the second division, viz., cases of prolonged or

continuous sleep. The light they throw on those of the first group is oblique and indirect, and by itself but fitfully illuminates an obscure subject.

In 1900 a case of prolonged sleep associated with a basal cerebral tumour was published by Soca [78]. The patient was a girl of 18; during seven months "*la malade dormait toujours, toujours de son sommeil paisible, d'aspect parfaitement naturel, toujours se reveillant facilement aux provocations ordinaires.*" The tumour was subsequently found to have penetrated into the third ventricle, and to have destroyed completely corpora mamillaria, tuber cinereum, chiasma and optic nerves.

Righetti's [72] case (1903) was that of a boy of 12, in whose case similar prolonged sleep was by far the most prominent symptom; "*fino dell' ammissione il paziente e in uno stato di sonno continuo. La sua fisionomia appare calma, il respiro e regolare come quello di una persona sana che dorma.*" When called in a loud voice he would wake up, sigh, and fall asleep again. In this instance the tumour completely destroyed optic nerves, chiasma, bandelette, and tuber cinereum, while the walls of the third ventricle were distended. Basing his researches to some extent on statistics furnished by Schuster, Righetti collected 775 cases of verified cerebral tumour, of which 115 were noteworthy clinically for the occurrence of pathological sleep. He compiled the following figures, which I have embodied in a table.

TABLE 1.

Site of tumour					Percentage of cases showing abnormal sleep
Thalamus and third ventricle	..	..	..	..	34.7
Medullary ..	..	..	..	..	27.9
Hypophysis and vicinity ..	..	..	..	..	26.5
Corpora quadrigemina and epiphysis ..	..	..	..	..	25.6
Cerebellum ..	..	..	..	..	15.8
Central gyri ..	..	..	..	..	10
Frontal ..	..	..	..	..	6, &c.

From these figures it is at once obvious that tumours situated in relation to the third ventricle (walls, floor, anterior and posterior extremities) together form a far higher percentage of abnormal sleep cases than any other group, and the association must be of significance.

Purves Stewart [83] published four cases of "tumour in the hypophysis cerebri" in 1909, and of these three were characterized by the occurrence of intense drowsiness, sometimes paroxysmal, lasting for hours, days, or weeks at a time. "In Case 1, and less strikingly in Case 4, the drowsiness had curious intermissions, during which the patient woke up for a time and was apparently clear and alert."

From the pathological descriptions the reader will find that while the pituitary itself was not invaded in all, the one common site of involvement was precisely the floor of the third ventricle.

Both before, and since, analogous cases have been put on record; present-day German writers on the subject confine their quotations largely to the recent cases of Pette [65], and Lucksch [48], which are not as a fact by any means so striking as some of those of which a précis is here furnished. Weisenburg [91] collected thirty cases of "tumours of the third ventricle" and found that "a decided tendency to drowsiness or somnolence" was specifically noted in sixteen, most of these being situated in the floor.

To correlate clinical and pathological findings in cases of cerebral tumour must be undertaken circumspectly; the effects of pressure, of oedema, of toxicosis, cannot be ignored, on the one hand, and, on the other, intracranial growths are commonly in the event too large for conclusions of localizing worth to be drawn therefrom. Thus it is that a tumour away from the third ventricle may be associated with somnolence or hypersomnia; in a case recorded by Bychowski [8] it was situated on the under surface of the left frontal lobe. Every neurologist can from his own experience quote cases of cerebral tumour of this kind; I may cite a single case of my own, in which the clinical symptoms closely resembled those of epidemic encephalitis as far as sleepiness and attacks of sleep were concerned, while the tumour proved to be located in the middle of the corpus callosum. Nevertheless the general conclusion holds, that basal tumours behind the chiasma are more likely than others to manifest themselves, *inter alia*, by hypersomnia.

It is equally hazardous to attempt to draw deductions from cases of cerebral abscess or of cerebral arteriopathy, for reasons which must be apparent. The evidence derived from epidemic encephalitis has been marshalled more particularly by Economo [20], whose general conclusion is to the effect that lesions in the vicinity of the third ventricle (floor, periventricular grey matter, region of the iter Sylvii) are responsible for the disorders of sleep that are highly characteristic of the average case of that disease.

SLEEP CENTRES AND THEIR LOCALIZATION.

Pathology can contribute comparatively little *specific* evidence, as we have just seen, but there are collateral lines worth scrutinizing. Of these one that appears to have some importance is the experimental,

though the data are rather meagre even if significant, and also now somewhat old.

Perhaps the most valuable work is that of R. Dubois [18], whose results were published as long ago as 1896, and have been neglected by all recent writers on the subject. Dubois experimented on marmots, and proved that "vers la partie antérieure de l'aqueduc de Sylvius et du côté du plancher du troisième ventricule, il existe des centres respiratoires de ralentissement et d'accélération, d'où dépendent également l'hypothermie et le réchauffement, la torpeur et la veille." He regarded the "centre" as a "centre du réveil," which plays "un rôle prépondérant dans le mécanisme du sommeil. Seulement son action est indirecte; il n'agit pas par une sorte d'inhibition imprimée par lui au système nerveux ou par une excitation centrifuge plus ou moins généralisée." This "centre" regulates respiration and circulation and produces natural sleep by a process of "autonarcose carbonique." Reviewing his experiments in a later publication, the same author states [19] that "J'ai mis hors de doute par l'expérimentation sur les marmottes un centre de sommeil, qui est d'ailleurs le même que celui du réveil, et se trouve justement situé dans la région où les auteurs que je viens de citer ont observé des lésions pathologiques coïncidant avec un sommeil persistant et prolongé." To Dubois without question must be assigned priority for some of the evidence now attributed to more recent work on the third ventricle and its grey matter.

Experiments conducted by Cushing and Goetsch [16] on hibernating wood-chucks dealt mainly with the pituitary gland, and led these workers to attribute hibernation to "a seasonal physiological wave of pluriglandular activity." It seems possible from the description of their operative technique that they injured also the tuber cinereum and other basal ventricular ganglia. Be this as it may, they found histological changes, especially in the pars anterior of the hypophysis in hibernating animals, as had Gemelli [29] some years previously in marmots. The latter, however, did not ascribe the somnolence of his animals to the changes in the gland, which he did not regard as a hypothetical centre for physiological sleep. Advances in knowledge of the last few years render implication of the pituitary problematical for these sleep states, and seem to invalidate the speculations of those who, like Salmon [75], attributed hypersomnia to functional insufficiency of that body.

Evidence has gradually been collected in support of the general

view already mentioned, a view to which a consideration of certain tumour cases, encephalitis cases, and Dubois' experimental work leads, viz., that physiological centres related to the floor of the third ventricle and the region of the iter—centres in the hypothalamus—have somehow a connection with the process of sleep. Undoubtedly much of this localization remains purely hypothetical, though it may well be of heuristic value. In the midst of conjectures (for pathological proof is wanting) it is desirable that the researches of Stief [84] should be given proper weight; that observer has found constant, marked changes in the nucleus paraventricularis, and in the hypothalamus generally, in cases of general paralysis, senility, cerebral arteriosclerosis, various kinds of psychosis, cachectic states, &c., and while he believes they explain the development of vegetative symptoms, and possibly the onset of the senium, there is no mention of sleep as forming a feature of any of his cases. For the present, therefore, exact pathological knowledge does not take us very far along the road to a solution of the problem of what mechanism or mechanisms are responsible for the symptoms of narcoleptic patients, or of where precisely they are situated.

One of the major difficulties yet to be surmounted is constituted by our ignorance of the physiological processes underlying natural sleep. It is well not to ignore the extreme complexity of the factors, a point which of itself renders highly improbable the existence of a *solitary* "sleep regulation centre" localized with mathematical exactness towards the posterior-inferior end of the third ventricle. Sleep must be regarded as a complex physiological process, which can be influenced both by physcogenic and psychogenic excitations. Its actual phenomena comprise manifestations belonging to different series—respiratory, circulatory, muscular, sensory and psychical. To suppose all these varying phenomena to be somehow controllable by a relatively limited ganglionic centre puts rather a strain on physiological belief, even if some lines of evidence appear to indicate the possibility of a ventricular nucleus playing a definite though undetermined rôle in the *initiation* of the whole somatic process. We do not know whether this "centre" inhibits or releases, or what precisely are the mechanisms it controls. In view of these facts some of the contentions seriously advanced in recent communications will not bear investigation. Hirsch [38], for example, because his case of pathological sleep was found to be associated with an abscess of the left optic thalamus, says that "sowohl der mediale Teil des linken Thalamus opticus wie das in

der Nähe der Okulomotoriuskerne gelegene Höhlengrau "Schlafzentren im richtigen Sinne sind"! "Localization" of this crude kind requires no comment.

We may, for the moment, consider Pavlov's views (1927), based on his work on dogs in connection with conditioned reflexes, and see how far they take us towards an explanation of the phenomena of narcolepsy. According to him, "sleep is nothing but internal inhibition which has become diffused continuously over the entire cortex and has descended also to some of the lower parts of the brain." Thus he considers sleep to be of *cortical* origin, but in its usual form simultaneous involvement of *infracortical* centres takes place, as evidenced by "relaxation of the skeletal muscles (closure of the eyes, drooping of the head, sagging limbs, and body limply hanging in the loops of the stand)." If, however, "a complete inhibition [is] confined exclusively to the cortex, without a concurrent descent of the inhibition into the centres regulating equilibrium and maintenance of posture, (centres of Magnus and de Kleijn)," then a different form of "sleep" is observed; the animal "preserves an entirely alert posture . . . with wide open immovable eyes . . . remaining motionless sometimes for minutes and sometimes for hours. On changing the position of an extremity such extremity retains the new position." In other words, "the animal is in a state of catalepsy."

Interesting as these observations are, to what extent do they illuminate the problems of narcolepsy?

(1) As we have repeatedly observed, the "sleep" of the narcoleptic certainly in numerous instances does not conform to ordinary sleep, and in such cases there can be no universal cortical inhibition, with descent to centres regulating equilibrium and posture. Various examples of the narcoleptic keeping on his feet, nay, walking along, when "asleep," might be cited. To hold that in such cases the internal inhibition is confined to the cortex, subcortical centres remaining in activity, is illegitimate, for as we have just seen this physiological condition results, according to Pavlov, in catalepsy, which is signalized by absence of movement.

(2) Pavlov's experiments do not help us to understand the phenomena of cataplexy, unless by analogy we are to allow that internal inhibition might invade the "centres of Magnus and de Kleijn" while the cortex is as a fact functioning normally, in the sense that the patient is conscious and in a state of awareness. If so, there is here no question of "descent" from cortex to mid-brain, and the speculation is physiologically unsupported, as far as Pavlov's experiments go.

On the other hand, I attach importance to his physiological explanation of catalepsy, which condition I have tried to show is unquestionably linked to narcolepsy. The passing attacks of immobility, trance-like states, distinguishing more than one of my own cases and noticed also in others, receive here a possible elucidation.

PATHOGENESIS.

At this point it is well, I think, to recapitulate from the clinical aspect the salient features of narcoleptic cases, lest any preconception of what is implied in the term "sleep" should mislead us.

(1) In the great majority of instances the *nocturnal* sleep of the narcoleptic is normal. We must, therefore, consider that we are dealing with mechanisms that are disordered only during the day, and not at night. This fact of itself disposes of the contention that in our first clinical division of narcoleptic cases any structural impairment, or any more or less permanent abnormal physiological state of the mechanisms concerned, is in existence.

(2) "Sleep" is a complete misnomer for the attacks in a large number of cases. In many, the patient is not asleep, but motionless and aware of his surroundings.

(3) A whole clinical group is constituted by cases in which attacks both of sleep and of tonelessness occur. Not only are these in reality less separable one from the other than appears on superficial consideration, but emotional excitations sometimes cause one to develop, sometimes the other. Again, the toneless attacks may supervene without obvious affective antecedent, as may the sleep; on occasion, one may be exchanged for the other.

(4) All gradations are met with, from narcolepsy without cataplexy, to cataplexy without narcolepsy.

(5) An outstanding clinical feature of both types of seizures is their relative brevity, their diurnal periodicity, and the rapidity with which the patient recovers from them.

With these considerations in mind, we may in conclusion attempt an approach to the problem of pathogenesis.

I am in accord with previous observers who have commented on the fact that affective hypotonia is seen from time to time in normal people, or who have referred to the embodiment in colloquial terminology of the existence of emotional influence on body musculature. Affective *Tonusverlust* certainly occurs unspecifically in many ways. From this viewpoint, its occurrence as a feature of narcoleptic syndromes

is merely an exaggeration of the normal, and forms a difference in degree and frequency but not in kind. Laughing, tickling, fright, fear, may in the normal person lead to a helpless, toneless, motionless state of skeletal musculature. German writers refer to the *Totstellreflex* of the frightened animal, "frightened out of its life," as we say. Allusion was made above to the occurrence of sphincter relaxation during the cataplexy in one of Redlich's cases; this also can scarcely be judged pathological if we recall certain slang expressions that seem to be common to many races ("auch besteht im Hollandischen ein Volksausdruck welcher sich auf die Inkontinenz beim Lachen bezieht."—Janzen). A patient under the care of Brissaud [7] had a similar experience.

"Une dame lui annonce que son petit chien vient de mourir. 'Vraiment,' dit-il; 'oh! que c'est regrettable!' Est-ce le dernier mot 'regrettable' qui, par une sorte de suggestion, réveille en lui une série d'idées tristes? Toujours est-il qu'il se produit comme un déclenchement de tous les ressorts expressifs; la simple tristesse de la physiognomie entraîne les larmes; après les larmes, les sanglots; bien plus, ce malheureux homme n'est plus maître de ses sphincters."

Evidently, then, the affective or cataplectic attacks are not essentially pathological, and unlike anything seen in normal persons; on the contrary, the mechanism or mechanisms in activity at such times may on occasion be in action also under conditions that cannot be regarded as abnormal. In my opinion *this* is the main distinguishing feature between narcolepsy and ordinary epilepsy, considered as symptoms; the narcoleptic attack (either narcoleptic or cataplectic) reproduces a phenomenon to be seen also from time to time, in major or minor degree, in persons of normal neural function, whereas the epileptic attack does not. It is essentially abnormal, and not to be likened to any neural phenomenon seen under normal circumstances. To this differentiation I am inclined to attach considerable weight.

Clearly, in respect of the affective seizures, a mechanism of *general motor inhibition* comes into play, in whole or in part; its outward manifestation ranges from mere trembling at the knees to temporary abrogation of the functions of standing, moving, speaking; whether this universal inhibition closes motility from the side of innervation or of tonus, or both, is, as I have pointed out, difficult to determine and in one sense relatively immaterial. My examination of the physiological state during one of these attacks has shown the outfall of tonus to be so absolute as to cause disappearance of the knee-jerks. Where is this

Proceedings of the Section of Neurology of the Royal Society of Medicine.

President—EDWIN BRAMWELL, M.D.

Clinical Meeting held at the Maida Vale Hospital, on Thursday, November 10.

(1) *Epilepsy with Hemianopia.*

By W. G. WYLLIE.

FLORENCE C., aged 45, married. One living child; one died, aged 1 week, from diarrhoea; no miscarriages.

Complaint.—Attacks of drowsiness, with and without loss of consciousness. These commenced at the age of 13. The attacks then lasted about five minutes, during which she could move and hear others speak, but could not speak herself. She had about two attacks a day.

At the age of 17, had "inflammation of the brain" with pyrexia and loss of consciousness. There was no diplopia and she was not sleepy. Afterwards fits ceased until the age of 32.

Since aged 32 she has had attacks resembling *petit mal* in nature, controlled by luminal. There is always an aura of "feeling something in the throat," but no visual disturbances.

Twelve months ago noticed that she did not see the last two words of a line when reading, and that she tended to walk into things on the right side.

Her memory has been deteriorating during the last three years. No other symptoms are present.

Signs.—Very slight rotary nystagmus to both sides, not constant but definite when present. Right homonymous hemianopia present. Slight weakness of right side of face. No other physical signs.

Diagnosis.—Epilepsy and hemianopia.

X-ray of skull (stereoscopic). No bony changes to be made out.

Blood: Wassermann reaction negative; *Cerebro-spinal fluid:* Wassermann reaction negative; protein, '035 per cent.; cells 2; Lange, 0001000000.

(2) *Epilepsy with Hemianopia.*

By C. WORSTER-DROUGHT.

F. B., aged 45, complains of seizures and defective vision towards the right.

History.—The first fit occurred four years ago and consisted of sudden loss of consciousness, followed by some degree of aphasia and right hemiparesis,

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less, motionless awareness of numerous cases (both in "sleep" attacks and in cataplectic attacks), than to actual sleep.

It is useless to force our cases of "narcolepsy" into the category that seems suited to them unless they fit comfortably; the initial task of minute clinical observation and investigation is still far from reaching its end.

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kind, A; or by local direct action at its own level owing to the existence of local conditions, B; or by excitations derived from lower levels, C. The formular combinations $X \times A$, $X \times B$, $X \times C$ will represent states not differing materially in their outward clinical manifestations, but their respective pathogeneses will be of differing rank. To take an obvious clinical analogy, that of torticollis; this purely symptomatic condition may be pathogenically a tic (psychical), a spasm, an occupation neurosis, a paralytic reaction, a reflex neuralgic reaction. So one narcoleptic state may closely resemble another in externals, but be distinguished pathogenically by the source of its excitant element. In a given instance it may be the outcome of excitations of a psychological order, in others it is a sequel to local conditions of the same level, or to impressions extending from lower levels. And there is no reason to doubt that in the psyche itself there may be levels of function, so that the pathogenic possibilities are correspondingly increased.

Only in some such way as this can we find a possible interpretation for the diverse narcoleptic symptoms of the psychoneurotic, the post-encephalitic, or the sufferer from cerebral tumour, as well as of the patient whose case is classed as spontaneous or idiopathic.

CONCLUSIONS.

At various points throughout this discussion, the conclusions to which it appears to lead have been briefly indicated, and further recapitulation is unnecessary. Their tentative nature, however, must be fully admitted.

With unfamiliar conditions like the "narcolepsy" which some persist in calling a "disease," attempts at identification and at nomenclature should come last, not first. The many analogies which various narcoleptic syndromes offer to those usually termed epileptic are here examined without prejudice; differing in outward manifestation, they none the less are such as to suggest that a more or less similar physiology lurks behind each. What precisely this is, however, it is impossible at present to determine.

Again, narcoleptic phenomena on analysis turn out to exhibit close affinities to those not only of epilepsy but also of catalepsy, while it is also found that "sleep" is a term used with vagueness and indeed with inaccuracy in respect of many of the symptoms classed as narcoleptic. The suggestion is that greater significance (from the viewpoint alike of ætiology and of pathogenesis) attaches to the toneless, power-

centre of tonus, whose inhibition leads to universal atonia? Is it labyrinthine, cerebellar, mesencephalic, or pre-mesencephalic? The toneless sinking to the ground is distinctly reminiscent of the effect on the boxer of a blow on the point. To quote Sherrington [76]: "The 'knock-out blow,' where the lower jaw conveys concussion to the otocyst, reduces in a moment a vigorous athlete to an unstrung bulk of flesh whose weight alone determines its attitude, if indeed a reactionless mass can be described as possessing attitude at all." Is there loss of deep reflectivity in the minutes that follow the knock-out? Unfortunately I can find no observations to aid in determining the question. Certain it is that consciousness is not by any means always lost, so that the parallel between this state and that of affective cataplexy is sufficiently close physiologically. If merely for the sake of discussion we postulate a labyrinthine origin for the somatic symptoms, and assume the continuance of integrity of the volitional motor system which nevertheless is incapable of overcoming the absolute atonia of the moment, by what mechanism does emotion affect the labyrinth or its central representation? It is conceivable that we have here through disease stumbled upon a biologically old automatism, a defence-reaction in which immobility is of advantage to the frightened animal, "struck all of a heap." If this should seem a feasible speculation, why is the mechanism activated by the act of laughter in so many instances? Hysterical laughter sometimes covers fear, yet the explanation is surely insufficient otherwise.

In the attacks of "sleep," further, it is permissible to see a *generalized inhibition of muscular activity* (on a previous page I have already pointed out that in numerous recorded cases only the appearance of sleep is exhibited, the fundamental feature being inability to move a single muscle). I consider, therefore, that the clue to the phenomena of narcolepsy is to be sought in the direction of generalized muscle- and tone-inhibition. It remains for future study to elucidate the mechanisms by which sensory or affective excitations inhibit instead of arousing motor activities, as well as those through which "sleep" and trance-like states develop "spontaneously."

The problem of pathogenesis, however, may be regarded from another angle. If we take a constellation of nerve-cells at any given neural level, it is theoretically capable of being activated by excitations from the same or from a superior or inferior level, and presumably also of being inhibited. One can consider the sleep mechanism X as being capable of excitation by stimuli of a psychical or psychopathological

lasting for one week. The second attack occurred in August, 1926, but was milder in character. Since this date he has had eight further attacks, each one followed by dysarthria and weakness of the right arm and leg of one or two days' duration.

The attacks are preceded by a short aura of giddiness, and during the attack it is stated that he is cyanosed, that the right arm and leg twitch, and that he froths at the mouth; the tongue has also been bitten. No history of venereal disease or head injury, and no previous illnesses of importance.

Physical examination.—Pupils equal and react to light and accommodation, right homonymous hemianopia; fundi normal, other cranial nerves normal. Some loss of joint sense in right fingers and astereognosis right hand; sensation otherwise normal. Arm-jerks moderate and equal, abdominals brisk and equal; knee-jerks equal; right ankle-jerk slightly greater than the left. Plantar reflexes flexor. Occasional involuntary movements of the right hand, especially flexion-extension of right thumb, and some inco-ordination of the right hand; the left hand and both legs are normal. Other systems normal. Arteries not thickened and blood-pressure 150 systolic, 90 diastolic.

The Wassermann reaction is negative in both blood and cerebro-spinal fluid, and the latter normal in all respects. X-ray of skull shows no abnormality.

Dr. HARRIS said that the date of onset of the hemianopia in Case 1 was uncertain. He had seen the association of epilepsy with hemianopia in a case of chronic syphilitic pachymeningitis. He had also seen transient hemianopia lasting up to twenty-four hours, associated with epilepsy in cases of lesions of the cuneus.

Dr. PARKES WEBER hazarded the diagnosis of tuberoscclerosis; although there was no adenoma sebaceum, he pointed out that there were numerous naevi over the face.

Dr. CLOAKE pointed out a definite objective diminution of sensibility over the face and suggested the possibility of pituitary disease in Case 1.

Mr. CAIRNS emphasized the attack of drowsiness in Case 1, and suggested the diagnosis of tumour of the tuber cinereum.

(3) *Case of Peripheral Neuritis, followed by Thrombo-angiitis Obliterans with Gangrene.*

By A. FEILING.

Mrs. T., now aged 48, was first admitted to hospital in April, 1925, for weakness of the legs. She then stated that her feet suddenly "went to sleep" while in bed one night, and that since then (January, 1925) she had had pains in the feet and gradually increasing weakness of the feet and legs. Examination showed a definite weakness of the movements of both feet and ankles, with partial foot-drop and a steppage gait; the ankle-jerks were lost, while the knee-jerks were retained; there was tenderness of the calves and slight loss of sensation for light touch over the distal parts of both feet and legs. No other

abnormality, except that both hands and both feet were always cold. The Wassermann reaction was negative and the cerebro-spinal fluid normal. No cause for the neuritis was found. She gradually improved and was discharged in July, 1925.

She was readmitted in October, 1926, with the symptoms of Raynaud's disease in both the hands and feet. The ankle-jerks were still absent. In July, 1927, she had influenza, followed by gangrene of the left second and third toes, and on July 12 she was again readmitted.

The skin over all the toes was glazed and blue, and both feet were cold; the second and third toes of the left foot showed early gangrene, being purple in colour and stone cold. Pulsation was felt in both dorsalis pedis arteries and in the posterior tibial arteries. The ankle-jerks were still absent on both sides, but otherwise there were no abnormal neurological signs.

On July 18 Leriche's operation was performed on the left femoral artery in Scarpa's triangle. The artery was small in calibre; alcohol was first injected into the sheath, which was then stripped off over a length of $1\frac{1}{2}$ in.

By July 22 definite gangrene had spread to the sole and dorsum of the foot, and on September 1 amputation through the middle of the leg had to be carried out. The stump has healed slowly. About September 18 gangrene began in the toes of the right foot. This has been treated conservatively, and a line of demarcation has gradually formed without further spread of the gangrene.

Dr. F. PARKES WEBER thought that the gangrene in the two lower limbs was due to thrombosis in small arteries, complicating angiospastic disturbance of Raynaud's type. He therefore suggested the diagnosis of "peripheral neuritis, followed by Raynaud's angiospastic phenomena and gangrene."

Professor BRAMWELL inquired whether muscular wasting ever followed occlusion of the femoral artery.

Dr. PARKES WEBER replied that such an occlusion might be followed by two types of wasting: (1) due to disease; (2) due to the same cause as the original femoral thrombosis.

Dr. CLOAKE asked for the experience of the Section on the result of Leriche's operation in Raynaud's disease. He had observed one case which benefited considerably.

Dr. CAWADIAS' experience was that the results of Leriche's operation in Raynaud's disease were good in 50 per cent. of the cases. In one case of true thrombo-angitis obliterans the result was bad, but there was a definite constitutional factor present. Of cases of obliteration secondary to infective arteritis (following influenza or typhoid), he had had no personal experience, but surgeons had told him that local procedures may benefit when the exact level of the occlusion was known. This level might be determined by means of oscillometry.

Dr. HARRIS referred to a case of syphilitic cerebral thrombosis followed by chronic thrombo-angitis obliterans, in which a bilateral Leriche operation had been of extreme benefit.

(4) *Chorea of Huntington's Type--Possibly Post-encephalitic in Origin*

By C. WORSTER-DROUGHT.

C. J. C., aged 29, complains of general weakness, slowness of movement, rapid fatigue on exertion and severe headaches.

History.—At the age of 20, while serving in the Expeditionary Force in Egypt during August, 1918, he developed a pyrexial illness accompanied by lethargy. No definite diagnosis appears to have been made; malaria was considered, but a report states definitely, "No malaria parasites found." Several relapses accompanied by pyrexia occurred from this time until his return to England in February, 1920. Following this, he developed the symptoms of which he complains, which have since become progressively worse.

Physical examination.—Pupils equal and react normally. Optic discs normal; poor convergence of eyes; facial movements slow, with some right-sided weakness and labial and lingual tremors. Voice somewhat tired and monotonous. Abdominal reflexes normal; knee- and ankle-jerks brisk and equal; plantars flexor. Some degree of general muscular rigidity, incoordination of arms and a tendency to festination.

From time to time he exhibits atheto-choreic movements of the head and limbs. All movements are very slowly and deliberately performed, and frequently preceded by slow, writhing choreiform movements of the arms and trunk or slow gesticulations, particularly on rising from a chair or beginning to walk. Heart, lungs, and other organs normal. Mentally, he exhibits slow cerebration and some dullness, and frequently falls asleep by day when sitting.

Dr. CARMICHAEL suggested the diagnosis of hysteria.

Dr. R. M. STEWART agreed that one had to exclude an element of hysteria from the gait.

Professor BRAMWELL said that the appearance of the tongue suggested post-encephalitic Parkinsonism.

Dr. ADIE said that the whole attitude of the patient, together with his disordered respiration, was suggestive of encephalitis.

Dr. WORSTER DROUGHT said that hysteria had been considered as a diagnosis, but that treatment accordingly had been of no avail.

(5) *Facial Hemihypertrophy; Neuro-fibromatosis; Kyphoscoliosis; Compression Paraplegia.*

By W. RUSSELL BRAIN.

Previous history.—N. S., aged 26, is said to have been normal at birth. Enlargement of the right side of the head and deformity of the spine have gradually developed since the age of 2. The vision of the right eye was lost at the age of 10. Seven weeks ago he first noticed weakness of the lower limbs, and three weeks later he was admitted to the London Hospital with paraplegia and acute retention of urine. The family history is normal.

Present condition.—His intelligence is normal. The whole of the right side of the skull is larger than the left, with special prominence of the temporal crest, the maxilla and the mandible. There is hypertrophy of the skin and subcutaneous tissues of the right side of the face, leading to occlusion of the right palpebral fissure and the right external auditory meatus. The right eye exhibits secondary glaucoma and staphyloma. There is hypertrophy of the gums on the right side, of the right half of the hard palate, and of the right side of the tongue, the papillæ of which are enlarged. The bones of the right upper limb are slightly larger and longer than those of the left.

There is a chain of neuro-fibromata above the right zygoma. The cutaneous pigmentation ranges from slight freckling of the face and neck to coffee-coloured patches 2 or 3 in. in diameter on the left knee.

There is extreme kyphoscoliosis and "pigeon breast." The cranial nerves and upper limbs are normal. There is marked weakness of the lower limbs, the right being more affected than the left, with extensor spasticity and bilateral extensor plantar responses. Relative anæsthesia to cotton-wool over both lower limbs; relative analgesia to prick over both sides of the trunk below the nipples and over the left lower limb; and some loss of postural sensibility in the toes, which is more severe on the right side than on the left. There is now only slight difficulty in beginning micturition. Radiographs revealed thinning of the cranial bones.

Dr. F. PARKES WEBER thought that all the features of the case might be regarded as manifestations of von Recklinghausen's neuro-fibromatosis. The cutaneous pigmentation was typical, but the kyphoscoliosis was of extreme degree. The tongue showed a minor variety of the rare "neuro-fibromatous hemihypertrophy," without a palpable plexiform neuroma. The hanging skin on the right side of the jaw might be called "neuro-fibromatous dermatolysis." There was neuro-fibromatous thickening of the gums on the right side of both the upper and lower jaws, and there was neuro-fibromatous thickening of the periosteum over portions of the skull, with palpable ossification of part of the thickened periosteum. He thought that the diffuse connective-tissue thickening in the skin and periosteum was allied to plexiform neuroma, the connective-tissue increase in the affected parts occurring with only slight neuromatous thickening. He thought that the patient manifested in a lesser degree the changes which were so remarkable in the famous "elephant man" of the London Hospital.

Dr. CRITCHLEY stated that he had seen subperiosteal swellings in at least two other cases of von Recklinghausen's disease, and stated that they had been specifically described as "subperiosteal cysts" by Barney Brooks and Lehmann, in 1924. Pathologically they were due to cystic degeneration occurring in small neuro-fibromata on the subperiosteal nerve filaments.

Dr. ADIE referred to the thickening of the eyelid, which together with an extreme degree of kyphoscoliosis had been the only manifestation of von Recklinghausen's disease in a young patient of his.

(6) *Case of Cortical Epilepsy of Obscure Ætiology.*

By E. B. STRAUSS.

W. P., boy, aged 12. Physical development that of a boy of 16. Has suffered from fits on and off since the age of 7 years. Was admitted into the Maida Vale Hospital for the second time last June, suffering from ten to twenty fits daily, which lasted for about a minute. Consciousness appeared to be retained. The eyes were turned to the right, and the head and trunk to the left.

During the fit there was a marked hypotonia of the right arm and leg, and athetoid movements of the right arm and hand. At all times there was a definite right hemiparesis and hypotonia of the arm and leg. The plantar responses were variable. The fits could only be controlled with chloral hydrate gr. xx *ter in die*.

July, 1927, operation to expose left parietal region. Apart from abnormal adherence of the meninges to the cortex and a very dilated vein, nothing abnormal was found. The meninges were partially separated and the wound closed. The patient made a slow recovery and remained in a very peculiar torpid mental state for some weeks. He has remained completely free from fits without drugs since the operation, but for some weeks following the operation the right hemiparesis was more marked than before. On discharge he was mentally normal. There was some protrusion of the dura mater through the wound. He has now completely recovered from his right-sided weakness and hypotonia.

Dr. WORSTER DROUGHT raised the possibility of a subcortical venous angioma with adhesion to the overlying meninges.

Dr. CARMICHAEL suggested the diagnosis of cerebral circumscribed meningitis.

Dr. FEILING said that the surgeon who performed the operation thought the appearances were unlike those of a venous angioma, and resembled rather a chronic inflammatory process.

(7) *Subacute Combined Degeneration of the Cord. Recent Blood Crisis with Rapid Recovery following Treatment with a Liver Diet.*

By DOUGLAS MCALPINE.

Male, aged 48, attended the Middlesex Hospital in June, 1923, with symptoms of subacute combined degeneration of the cord.

The chief nervous symptoms were: (1) Slight paresis both lower limbs; (2) absent knee-jerks; ankle-jerks feebly present; (3) vibration sense diminished in lower limbs; (4) plantar responses flexor.

Blood-count.—Red blood-corpuscles, 2,900,000; hæmoglobin, 80 per cent.; colour index, 1.4. No nucleated red cells. Wassermann reaction negative.

January, 1924.—Neurological signs as before. Red blood-corpuscles, 3,900,000; hæmoglobin, 80 per cent. colour index, 1.0.

July, 1924.—Fractional test meal showed total achlorhydria; knee-jerks and ankle-jerks absent. Treatment with full doses of dilute hydrochloric acid begun.

January, 1925.—General condition had improved; working full-hours in a shop. Red blood-corpuscles, 4,300,000; hæmoglobin, 84 per cent.; colour index, 1.0. During 1925 and 1926 condition remained satisfactory.

May, 1927.—Severe blood crisis. Treated at home. Blood transfusion necessary. Patient not seen again until September 23. He stated that progress had been very slow. Blood-count (September 23, 1927): Red blood-corpuscles, 2,150,000; hæmoglobin, 50 per cent.; colour index, 1.2. Nucleated red cells, 1.5 per 100.

September 9, 1927.—Liver treatment begun; $\frac{1}{2}$ lb. per diem.

October 15, 1927.—Patient stated he felt much better since taking liver. Appetite had returned, palpitation had disappeared, and that he felt as well as before his relapse in May. He had returned to work, and could walk a mile or so without fatigue. Blood-count: Red blood-corpuscles, 3,040,000; hæmoglobin, 54 per cent.; colour index, 0.9. No nucleated red cells seen.

November 4, 1927.—Improvement has continued. Right knee-jerk feebly present, left absent. Left ankle-jerk feebly present, right absent. No paresthesia in legs. Plantars remain flexor. He has gained 9 lb. in weight since liver treatment was begun. Blood-count: Red blood-corpuscles, 3,870,000; hæmoglobin, 82 per cent.; colour index, 1.1; megalocytosis is present.

The knee-jerks are now obtainable; the right plantar is extensor, and the left one flexor. He also quoted two other cases of subacute degeneration treated by liver extract, and emphasized the importance of treating dental sepsis, and also of allowing for spontaneous remissions.

Clinical meeting held at the National Hospital, Queen Square, Bloomsbury, on Thursday, January 12.

(1) *Thyroid Neoplasm with Secondary Deposits in Skull.*

By J. S. COLLIER.

E. E., male, aged 59.

This patient gives a history that fifteen years ago a swelling appeared in his neck. It was painless and grew slowly but steadily. Five years ago the swelling had become so large that he was dyspnoic and had difficulty in swallowing. He was operated on and most of the thyroid gland was removed. He improved and returned to work.

Four years ago he noticed a small lump in the right parietal region. This has grown slowly but steadily and is now tender.

In August, 1927, he again began to have difficulty in swallowing. His breathing was now worse when he was lying flat.

General condition.—Slight stertor as he lies in bed. Gross dyspnoea on exertion.

Cranial nerves.—Pupils unequal, right $3\frac{1}{2}$ mm., left 2 mm. They both react briskly to light and on convergence. Visual acuity $\frac{6}{12}$ both eyes. Fundi normal. The right palpebral aperture a little wider than left. Right eye displaced slightly down and up.

Motor and sensory systems normal.

Reflexes.—Normal, except that the left ankle-jerk is absent, but he had sciatica sixteen years ago.

Skull.—There is a rounded hard mass in the right parietal region which rises smoothly from the general skull surface. There is a soft area at the top of it which is tender to pressure.

Cardiac system.—The apex beat is $5\frac{1}{2}$ in. from mid-line. Diastolic shock over the aortic area. There is some extension outwards of dullness in the second right space. Heart sounds: there is a short harsh systolic murmur accompanying the first sound over the aortic area. The aortic second sound is ringing and accentuated.

Blood-pressure: Left arm 146/78; right arm 158/92.

Cerebro-spinal fluid: Normal.

Dr. WILKINSON said that the first suggestion was that the cranial tumour was gummatous, the spinal fluid and blood Wasserman reactions were both negative, however. It was now suggested that the skull lump was independent of the thyroid tumour.

Dr. FEILING asked what evidence there was that he had ever had an actual neoplasm of the thyroid.

Dr. WILKINSON said that there was no proof beyond the patient's statement to that effect.

Dr. ADIE said he first saw the patient six weeks ago, and he had thought the swelling was a gunma.

(2) *Epilepsy following Contusio Cerebri.*

By J. S. COLLIER.

F. K., male, aged 12.

This boy gives a history that in August, 1925, he fell 17 ft. and struck his left occiput and left mastoid region. He was picked up unconscious. He remained so for ten days. On recovering consciousness he was completely blind for two days—his sight then returned.

There was no bleeding from mouth, nostrils or ears. He remained in hospital three months.

In May, 1926, nine months after the accident, he had a fit. He fell suddenly in the street and his limbs were convulsed. His lips went black and he frothed at the mouth. He wetted himself but did not bite his tongue. He remained unconscious for ten minutes.

In November, 1926, he had another fit of the same type. In March, 1927, he had another attack—this attack was preceded by an elaborate visual aura. He states that in the left visual field he sees people walking past him. They move from left to right across the field and he can still see them if he closes

the right eye. He can distinguish men from women in the crowd, but cannot tell the colour of their clothes. Their faces are fairly clear, but he does not think he would recognize them in real life. He has never heard them speak—they pass for from three to five minutes. Then his hands and fore-arms begin to jerk and he falls unconscious to the right.

On October 14, 1927, he had another attack at school. This was preceded by a similar aura and the attack then followed its usual course. Every attack has been succeeded by vomiting and headache.

He wetted himself in the first one only, and has not bitten his tongue in any of them. Between the attacks he has been in normal health.

Cranial nerves.—Pupils unequal, right 4 mm., left $5\frac{1}{2}$ mm. The left reacts briskly to light, and on convergence Right. There is the tiniest flicker to bright direct and consensual light. The right pupil reacts well on convergence. Fundi normal. Left visual acuity $\frac{6}{6}$, right $\frac{6}{9}$. External ocular movements normal. No nystagmus, diplopia, or en- or ex-ophthalmos. Right half of face acts a little better than left in both upper and lower halves.

The motor and sensory functions and all the reflexes are normal

Respiratory system normal.

X-rays of his skull suggest a fracture in the right occipital region.

Sir J. PURVIS STEWART said an "occipito-temporal fracture" would be a correct designation; the skiagram showed that the fracture involved the temporal bone, and the character of the visual aura suggested a temporal site. Absence of a quadrant field defect suggested a cortical lesion.

Dr. C. P. SYMONDS wondered whether the site of the fracture was independent of the site of the cerebral contusion. He had thought that the lesion was in the neighbourhood of the thalamus, and that the hallucinations were due to disturbance in the optic radiations rather than in the temporal lobe.

(3) *Polycythæmia with Cerebral Thrombosis.*

By C. M. HINDS HOWELL.

S. N., aged 29, suddenly developed a right-sided paralysis three months ago. It came on while he was at work, and was unattended by loss of consciousness. This attack lasted only a few minutes, and he felt quite well afterwards. A second attack followed fifteen minutes later, and in this one his speech became affected. Four more transient attacks occurred before the evening. The following day he had another severe attack, which was followed by a permanent right-sided weakness.

The right hemiparesis is now improving; speech is almost normal. Spleen enlarged. Blood-pressure 135. Red blood-count 12,000,000.

Dr. CRITCHLEY said he had had no experience of a cerebro-vascular disorder associated with polycythæmia.

Dr. SYMONDS states he had seen one case of a vascular disorder in this disease. Later the patient had died from some intercurrent disease, and an old hæmorrhage into the brain was found at the autopsy.

Dr. F. PARKES WEBER regarded the case as a typical one of erythræmia (splenomegalic polycythæmia). Cerebral thrombosis had been early recognized as an occasional complication (e.g., case of Hutchinson and Miller, 1906). He thought that the white blood-cells should be counted and a differential count made in every case of erythræmia, so as to distinguish the cases bordering on myeloid leukæmia—the so-called cases of “erythro-leukæmia” (Guglielmo) and “subleukæmia erythræmia” (Aubertin). (Compare F. P. Weber and O. Bode, “Erythro-Leukæmia and Blumenthal’s Disease,” *Med. Press*, London, 1927, vol. clxxv, p. 174)

If a trial of phenylhydrazine treatment were made, care should be taken to discontinue the drug when the erythrocyte count fell as low as 5,500,000, as a further fall was likely to occur during seven to ten days following the termination of the treatment.

(4) *Schilder’s Disease (?)*.

By E. A. B. PRITCHARD.

A. A., male, aged 12. This boy, who is the youngest member of a family which shows a tendency to mental deficiency in the males and average intelligence in the females, developed normally until he had an accident at the age of 3½ years. Since this time there had been a gradual deterioration in several respects. His speech became slurred, and is now limited to meaningless sounds; his hearing has deteriorated, so that it is now doubtful whether he can hear at all, and he certainly cannot understand spoken words, while his general movements have become awkward and irregular, with increasing spasm and athetoid movements of the trunk and limbs. One aunt had become prematurely deaf; his mother was very deaf. The patient was the sixth of seven children; his three sisters were of very bright mentality; the three brothers were extremely dull. The diagnosis of an unusual variety of Schilder’s disease had been suggested.

Dr. SYMONDS referred to a case of familial Schilder’s disease he had shown one year ago. Ferraro had since then published three cases of familial Schilder’s disease. Krabbe’s description of a variety of diffuse cerebral sclerosis presented the pathological picture of this same disease. This particular patient corresponds with the description of the Pelizaeus-Merzbacher syndrome, a disease in which males only were affected. The query again arises as to whether Pelizaeus-Merzbacher’s disease and Schilder’s encephalitis were not one and the same disorder.

(5) *Palato-Laryngeal Nystagmus*.

By S. A. K. WILSON.

A. B., aged 53, was admitted for weakness of his left arm and leg, failing sight and bad memory, of twenty-four months’ duration. Sudden onset twenty-four months ago, on waking one morning, of weakness of his left arm and leg, from which he made a gradual recovery. Three months ago he suffered with

severe headache, and a day or so later became suddenly blind whilst in the street; this persisted for two months and sight has since gradually returned.

A week later he had a "stroke," heralded by a fit in which there were right-sided convulsions. Speech was lost for three days, but there is no history of subsequent motor weakness. Memory has recently become very bad.

Physical examination.—A patient of poor mentality; memory bad, co-operates poorly but is well-orientated. Speech is indistinct. His pupils are oval, and left greater than right, but both react normally. The retinal vessels are tortuous, with indentations of veins by arteries and pigmentary changes at the maculae. Palatal nystagmus is present. This is regular in rate; on admission the movement was at the rate of about 144 per minute, but is now slower, about 116 per minute, and takes place in a vertical direction. In addition there is a horizontal nystagmoid movement of the left superior constrictor muscle, and of the left posterior faucial pillar. There is slight horizontal nystagmus of the right superior constrictor muscle. The palate moves poorly, but equally and symmetrically; the palatal reflex is normal. The tongue is protruded to the right and is tremulous but not wasted. The left limbs are weak and the tone of their muscles is increased, but there are no sensory changes. The reflexes are exaggerated but equal in both upper limbs. The abdominal reflexes sluggish in the upper and absent in the lower quadrants. The right and left knee- and ankle-jerks are exaggerated and there is ankle-clonus on both sides, but the plantar responses are flexor. Some precipitancy of micturition exists. The heart is not enlarged, but the aortic second sound is accentuated. Blood-pressure is 190/112.

Examination of vocal cords shows well-marked twitchings of the left arytaenoid and left vocal chord, synchronous with those of palate. There are no involuntary movements on the right side.

Examination of the cerebro-spinal fluid reveals very slight increase in protein content only. Wassermann reaction is negative. The Lange test shows no change.

Sir J PURVES STEWART suggested that the term "myoclonus" was preferable to "nystagmus" to describe the involuntary movements present in this case.

Dr CRITCHLEY stated that this variety of movement appearing in the palate, pharynx and larynx was not very uncommon in cerebro-vascular disease. In view of the diffuseness of the lesion, it was difficult in such to correlate the pathological and clinical observations. Palatal "nystagmus" had, however, been seen in numerous cases of focal lesions, such as in tumour of the cerebellar vermis (as in the first case recorded), in focal softenings in the dentate nuclei or in the pons. Dr. Wilson had spoken, in 1921, of a case of palatal nystagmus associated with tumour of the corpora quadrigemina. Dr. McAlpine and Professor Lhermitte had described choreic movements of the face, palate, and larynx which they associated with neo-striatal disorder. In the most recent work on this subject, Signorelli had implicated the substantia reticularis.

(6) *A Case showing Tonic Innervation.*

By C. P. SYMONDS.

L. H., aged 15, first came under observation at the age of 12, in November, 1924. The mother stated that, having been previously healthy, a year before it was noticed that she was using her left hand more than her right, and that she tended to swing her right leg as she walked, wearing out the toe of her right boot. For the past month she had been complaining of headaches when waking in the morning.

On examination, there was slight weakness of the right side of the face, and the right arm and leg, with diminished abdominal reflexes on the right side. The plantar responses were both flexor. Nystagmus was noted on conjugate deviation to the left. The Wassermann reaction in the blood was negative. X-rays of the skull were negative. X-rays of the chest showed a large gland at the right root and some rounded opacities arranged in streaks, suggesting some infiltration of the lungs.

She was admitted to hospital, where no further physical signs were discovered. Her visual fields were full on the perimeter. There was no aphasia.

On the suspicion of a tuberculoma in the brain-stem she was discharged to a convalescent home at Broadstairs. There she remained for six months.

On her return in June, 1925, she attended for re-examination. The weakness and physical signs remained as before, but she was free from headaches, and she returned to school.

Two years later, in June, 1927, she began to complain of frontal headaches. After this had continued for a fortnight, she was seized one morning while at stool with sudden severe pain in the head, vomited, and within a quarter of an hour became unconscious.

Five and a half hours later she was admitted to Guy's Hospital in a semi-comatose condition. There was well-marked cervical rigidity and bilateral Kernig's sign. The abdominal reflexes were with difficulty obtained on the right side. The right plantar response was extensor. The right big toe occasionally went into a position of extreme dorsiflexion with the foot in a position of plantar flexion, this posture being strongly maintained for half a minute at a time.

Lumbar puncture gave an evenly blood-stained fluid with the characteristic appearances of a spontaneous subarachnoid hæmorrhage. This was not recognized as such at the time, and further lumbar punctures were done on the subsequent day and again two days later under the impression that the hæmorrhage was accidental. On each occasion the appearances were the same, except that with the passage of time the supernatant cerebro-spinal fluid standing in the test tube became more definitely golden-yellow in colour.

Four days after admission she was able to co-operate in a complete examination. There appeared to be some slight difficulty in speech production. There was weakness of right face, arm and leg, but no sensory disturbances.

It was noted that "when the fingers of the right hand are clenched the patient has great difficulty in initiating relaxation, and attempts to start this movement with the aid of her left hand."

Seen on the fifth day of her illness, she showed bilateral papilloedema of moderate degree, with a few small retinal hæmorrhages, in addition to the other physical signs already described. The papilloedema continued to increase during the next three or four days. Her temperature was raised for the greater part of a week. The right-sided weakness improved, and the right plantar response became flexor.

On July 8 Dr. Ironside noted Meyer's reflex present on both sides, exaggerated on right. "On stroking the palm in the region of the carpo-metacarpal joints on the right, the fingers go through two or three movements of alternate flexion and extension, and the hand moves slightly towards the stimulus applied to the palm."

The difficulty in relaxing the right-hand grip improved. The patient's general condition rapidly became normal, and she was discharged on August 8.

Since then she has been completely free from headaches, and in good health, apart from the continued slight hemiparesis and "tonic innervation" of right hand and foot.

Present condition.—General health is good and physical development and mental state normal for her age. She is right-handed; no left-handedness in family. No speech defect is discovered on receptive or productive sides. The visual fields are normal to rough tests. Optic discs are both pale with clear-cut eyes. (Probably consecutive atrophy following the papilloedema noted above.) The pupils are equal and central, the right a little irregular; they react normally to light (direct and concentric) and on accommodation. The ocular movements are full with nystagmus, fine to right, coarser to left. The corneal reflexes are present and equal. There is weakness of the right lower half of the face, equally present in voluntary and emotional movement. The palate moves in mid-line and the tongue is protruded centrally. In the right upper limb individual movements of the hand and fingers are good, but power is less than on the left. Consecutive quick movements, e.g., piano-playing, are slow. There is some spasticity of the flexors of wrist and fingers. In all positions of the trunk and limbs the right hand is held slightly flexed and adducted to the ulnar side. This is perhaps most apparent when the hands are held above the head. When the hands are held outstretched with fingers spread, the same postural abnormality is to be observed, associated with irregular jerky movements of adduction and abduction in the fingers.

When she grasps the observer's hand firmly there is increased flexion and ulnar adduction at the wrist, with some difficulty in relaxing the grasp owing to persistent tonic contraction of the flexors, which can be seen and felt in the fore-arm. The same difficulty is much more marked when she makes a fist. It may be as much as half a second before she can relax the flexors, in spite of powerful contraction of the extensors during this time. The effort to open the fingers is associated with increased flexion and adduction of the wrist. After

she has opened and shut her hand two or three times the difficulty in relaxing the flexors becomes less, but is usually as well marked as ever after a rest. Other movements of the right upper limb are normal, with no difficulty in relaxation. The triceps, biceps and supinator reflexes are all more easily obtained on the right than the left. Stroking the palmar surfaces of the right fingers over the proximal phalanges, from ulnar to radial border, occasionally provokes a slight adduction of the thumb, not to be obtained from the other hand. No postural reactions of the type described by Riddoch and Buzzard could be evoked from the right upper limb, nor could any alteration of postural tone be demonstrated by alteration of the position of the head.

In the trunk no weakness can be observed. The abdominal reflexes are all present and equal.

In the lower limbs there is slight spasticity and weakness of the flexors of the right ankle and toes. The patient states that she has observed the same kind of difficulty in relaxing the toes as the fingers. This can be demonstrated clearly by asking the patient to grip the observer's finger tip under her toes. There is a persistent contraction, apparently of the long flexors of the toes, which involves flexion of the ankle as well. The duration of the tonic after-contraction here is much shorter than in the case of the fingers. There is the same tendency eventually to obtain release by momentarily increasing the movement of flexion. The action is similar to that instinctively used to get rid of a cramp, though in the patient's case there is no pain. Other movements of the lower limbs are normal. The knee- and ankle-jerks are present and equal on the two sides; the plantar responses are flexor.

The sphincters and gait are normal.

Blood-pressure is 95 and 55.

No abnormalities have been detected in head or spine, or in any of the other systems.

Dr. CRITCHLEY stated that the description of the phenomenon, as given on July 8, suggested rather a "grasp reflex." The two phenomena of forced grasping and tonic innervation both occurred as constituents of the syndrome of the anterior cerebral artery. He suggested, therefore, that the lesion in this case resulted from an aneurysm of the anterior cerebral artery.

Dr. SYMONDS considered this the most reasonable explanation.

A Case of Familial Nervous Disease (Disseminated Sclerosis).

By C. P. SYMONDS.

aged 24, gives a history of difficulty in walking since 1921, fall in January of that year, after which she felt numb all down

came under observation as an out-patient at Guy's Hospital in 1922, when she showed left hemiparesis with indefinite sensory and nystagmus.

In the same year she began to have attacks, lasting two or three

minutes, in which she becomes completely disoriented in space, and has a feeling of impending disaster. She has never lost consciousness in these attacks, but cries out in fear. They come on suddenly at any time and without warning. She has never had one when alone.

In July, 1925, she first noticed diplopia, especially on looking to the left. At present she shows the following physical signs:—

Mentally she is somewhat childish. Speech is not abnormal.

There is a high degree of myopia, but the optic discs are normal.

The right pupil is larger than the left, but the pupillary reactions are normal. There is fine nystagmus on conjugate deviation to right and left. Diplopia is sometimes present when she looks to the left, but there is no demonstrable weakness of ocular movements. The left lower face is slightly weaker than the right. The remaining cranial nerves are normal.

There is no wasting or weakness of the upper limbs, but a tremor of the intentional type is present on both sides, being more marked on the left. Of the lower limbs the right is more powerful than the left. There is gross inco-ordination in the performance of voluntary movements, such as the heel-knee test.

There is no demonstrable organic loss of sensation, but there is a functional hemihypalgesia.

Triceps, biceps and supinator jerks are present and equal on the two sides. Of the abdominal reflexes the right lower only is obtained. Knee- and ankle-jerks present and equal. No ankle- or patellar-clonus. Plantar responses are both extensor.

There are no physical signs in the other systems.

The Wassermann test is negative in blood and fluid. The cerebro-spinal fluid is clear and colourless; cells 4 per c.mm., 5 per cent. large mononuclears; total protein 0.1 per cent.; Nonne-Apelt ++; Pandy +; Lange 0001101000.

Family history.—A brother died in 1926, at the age of 32, of a disease diagnosed as disseminated sclerosis. The symptoms began in 1921 with diplopia. In 1922 he had weakness of the legs and tremor of the hands, and it is recorded that he then had nystagmus, weakness of the right hand grip and an extensor plantar response on the right side. A note in 1923 records nystagmus and strabismus, spastic-ataxic gait, scanning speech, gross inco-ordination and intentional tremor.

One sister died, aged 35, two years ago. The date of onset of her disease is unknown, but in January, 1925, she had diplopia, exaggerated reflexes, extensor responses and absent abdominal reflexes. The Wassermann test was negative in the spinal fluid and the gold curve normal.

This case had been reported in the *Lancet*, 1927, ii, 701, under the heading of Familial Disseminated Sclerosis. The suggestion is made that, in the absence of pathological evidence, this diagnosis must be regarded as doubtful. This case belongs to the group of familial nervous diseases of which the cerebellar ataxies and familial spastic paraplegia may be taken as examples.

Dr. WORSTER-DROUGHT referred to two sisters under his

symptoms resembling disseminated sclerosis. A third sister had died, with symptoms very like disseminated sclerosis.

Dr ADIE stated that he and Dr. Critchley had recently collected a number of cases of familial disseminated sclerosis. There was at least one case in the literature in which the diagnosis of disseminated sclerosis had been confirmed by autopsy. This case was described by the younger Hoffmann.

Dr. CLOAKE spoke of a similar family under his care. One member had symptoms resembling disseminated sclerosis with the characteristic disc changes. A sister was an even more advanced case; the previous generation also showed a nervous disorder resembling disseminated sclerosis.

(8) *A Case of Dermato-Myositis.*

By J. P. MARTIN.

Patient, Mrs. B.; aged 50.

History.—About thirteen months ago began to have difficulty in getting up from a chair and in raising her arms; these disabilities gradually increased, after a few months she was unable to stand, and when sitting had difficulty in holding up her head; for the last four or five months she had been confined to bed and has become thinner.

Present condition.—The skin on the lateral parts of the face, on the chest and shoulders, the right side of the abdomen and the anterior surfaces of the legs, and to a less extent on many other parts of the body, is thickened and bound down to the underlying tissues. The muscles of the shoulders and chest, the biceps brachii, the hamstrings and other muscles are hardened, and in the pectorals, biceps brachii and hamstrings there are contractures, sensation is everywhere normal, and there are no signs of disease of the central nervous system; the cerebro-spinal fluid is normal.

The patient is being treated with fibrolysin, massage and warm baths, and improvement is noticeable in the skin and muscles of the neck.

Gowers first described this condition, and later Oppenheim. The patient had recently shown some improvement.

Professor BRAMWELL referred to a similar case associated with facial hemiatrophy. This combination had also been referred to by Gowers.

Dr. F. PARKES WEBER said that the patient was very decided that the first symptoms were simple weakness, and not stiffness or pain, in the muscles, that was a strong point against the diagnosis of any kind of dermato-myositis or of sclerodermia. He suggested that the case was a rare form of chronic generalized symmetrical multiple peripheral neuritis in which the muscle fibres themselves, as well as the nerves, were involved. The subsequent hardening of the muscles and slight adhesion of the skin might be secondary. There was no obvious alteration in the texture of the skin itself.

The case described by Gowers was that of a woman, aged 36, whose first symptoms were a constant tired feeling and aching pain in the back and around the loins. Both nerves and muscles were thought to be involved—a poly-

neuritis accompanied the polymyositis, but the muscular affection was far more extensive than in case of pure polyneuritis (see Gowers; *Brit. Med. Journ.*, 1899, p. 65). The disease might be termed a *chronic symmetrical generalized neuro-myositis*.

Clinical Meeting of the Section of Neurology, March 8, 1928.

Discussion on the Narcolepsies.

Dr. S. A. KINNIER WILSON introduced the discussion by presenting to the meeting an abstract of his paper published on p. 63.

Dr. WORSTER-DROUGHT referred to an article published in the *British Journal of Psychology*, in which he described some of the earlier cases he had observed. At present he has four cases under observation; three men and a woman. In one of these, in which the toneless attacks commenced before the attacks of sleep appeared, he had been able to observe the patient during an attack; his head suddenly dropped forward, his lower jaw fell, and he suddenly became flaccid and powerless. While in this state his arm-jerks and knee-jerks could not be obtained.

He agreed with Dr. Wilson that narcolepsy should be regarded as a symptom-complex rather than as a disease, and it seemed to him that it is closely allied to the condition known as catalepsy.

Sir J. PURVES-STEWART referred to his observation several years ago of attacks of hypersomnia associated with lesions in the neighbourhood of the floor of the third ventricle. He has lately observed excessive sleep following inflation of the third ventricle with air. It seemed to him difficult to explain such paroxysmal phenomena as distinguish narcolepsy by the existence of a stationary lesion or functional disturbance in the brain.

Dr. GRAINGER STEWART said that during the last three years he had observed three typical cases of narcolepsy. One of these was particularly interesting as the narcolepsy developed in a child who was subject to epilepsy. At first while epileptic seizures still occurred, the child began to have typical cataplectic attacks, which were generally brought on by the first taste of food, which he assumed acted as an emotional stimulus. Later both the epileptic and cataplectic attacks ceased and were replaced by periodic attacks of sleep. In one cataplectic attack the knee-jerks were absent, but he could not elicit extensor responses, the plantar reflexes being either absent or indefinite.

Dr. PHILIP CLOAKE offered as an interesting contribution to the subject the record of attacks of sleep and cataplexy described by a girl under his care.

"I am 22 years of age: I first noticed a tendency to sleep unnaturally between the age of 19 and 20; even as I walked along I would fall asleep; several times I did not know even how I managed to get from one end of the work-room to the other; I would suddenly wake with a start and find that I must have been asleep. For at least six months every time I fell asleep while I happened to be in a sitting position, my head would fall back as far as

possible, and then flop right forward for at least a dozen times, and I was quite unable to stop it. As time went on I found that as soon as I lay down in bed I could not move or speak, and if I tried to speak I only made a muffled sound; but if anyone happened to come in the room and spoke I could hear what they said quite well, and if they passed in front of my eyes I could see them though my eyelids felt almost shut. I would have as many as six or seven of these attacks straight off, but each one would last only a minute or so.

"During the last eighteen months these turns have become stronger and it requires a greater effort to pull myself round; I have to make two or three attempts before I can do so, and then when I get up I usually jerk forward once or twice before I can steady myself, but except for feeling a little out of breath I am quite all right.

"I fall asleep at all times, even standing up at work, and I am so bad that I have to go out and talk to someone, or go out in the air before it passes off; and then more often than not during the next half hour I am just as bad. This will keep on perhaps all day, and then next day I only feel it once or twice. After this sleepy feeling passes off my eyes feel very sore.

"When I laugh my legs give way and I have to hold on to anything or anyone near or I should fall, also my eyes seem to roll about and for a minute or so all seems a blank, then everything seems muddled up and out of place, and I have to shut my eyes before I can see things plainly, and generally instead of seeing one I see two, this also happens if anyone takes me by surprise and I turn round quickly. I have to wait a minute or two before I can speak."

One special feature of this case is the curious state of mental confusion that followed the attacks. He was not aware that cataplectic attacks occur in symptomatic narcolepsy, as in that which occasionally follows encephalitis lethargica.

Dr. HENRY COHEN said he had observed eight cases of narcolepsy, in three of which the condition followed attacks of epidemic encephalitis. He was impressed by Dr. Wilson's emphasis on the affinity of narcolepsy to epilepsy, and his own observations tended to confirm this view. In one of his cases from twenty to thirty cataplectic attacks occurred each day, in fact any shock or unexpected noise might precipitate an attack. He had seen a case of congenital spastic diplegia in which a noise might bring on a similar cataplectic attack which was often followed by myoclonic twitchings. This case in many ways resembled that of a woman with congenital syphilis under his care, in whom sudden noises excited epileptic seizures. He had observed true cataplectic attacks, occurring usually after laughter, in a patient who had had epidemic encephalitis.

Dr. GORDON HOLMES referred to two cases of true narcolepsy, one a young man and the other a young woman, which he had seen. Neither of these presented any special features except that the man, whose case has been referred to by Dr. Wilson in his paper, had been subject to epistaxis before the narcoleptic symptoms appeared.

He had the opportunity of making an interesting, and, it seemed to him, an important observation in a middle-aged man, who probably has a slowly growing tumour in the hypothalamic region. He has lately increased greatly in weight and has become subject to attacks of indomitable sleep, lasting ten to forty minutes, from which he wakes up feeling quite natural. In addition he has had a few sudden and unexplained "collapses," or falls on emotion. His symptoms improved very much on the administration of large doses of thyroid and recurred when the dose was reduced. He referred to the case he had described of "Falling on Noise and Surprise" (*Brain*, 1927, **50**, 720), which seemed in certain ways allied to narcolepsy. This boy was from 5 to 14 years of age liable to fall flaccidly on noise and surprise; at the age of 14 years he had an epileptic attack, and since the case was recorded six months ago he has developed frequent and severe epilepsy.

Dr. R. D. GILLESPIE mentioned that in the case which he had observed slight emotional stimuli might excite an attack, while stronger emotions had often no effect. Hot baths also tended to cause attacks of sleep. In some of the attacks of sleep automatic activities might continue for a time, as writing. In one attack he found the knee-jerks absent and could not obtain the plantar reflexes. This case improved for a time under psychotherapeutical treatment, and later on large doses of hyoscine hydrobromate.

NOTICES OF RECENT PUBLICATIONS.

Conditioned Reflexes. An Investigation of the Physiological Activity of the Cerebral Cortex. By I. P. PAVLOV. Translated and edited by G. V. Anrep. Pp. 430. Oxford: University Press. 1927. Price 28s.

It is several years now since such a noteworthy contribution to physiology, and especially to neurological physiology, appeared in the English language as Professor Pavlov's book. We have been to some extent familiar with the trend and the general results of the investigations to which he and his school have devoted the last twenty-five years, but as almost all the publications on the subject have appeared in Russian and have been widely scattered in various journals, few English readers have had the opportunity of making a first-hand acquaintance with them. We are therefore under a debt of gratitude to Dr. Anrep, who has translated and edited the volume in which Professor Pavlov has collected for the first time the general results of these investigations. The translation itself is distinguished by a clear and concise style which frequently suggests to the reader an original work by a master of our language.

The book takes the form of a series of lectures in which the development of the subject is traced to a succession of general conclusions. In the first chapters we learn of the mode of production and the factors that influence the appearance of conditioned or acquired reflexes; then the various forms of inhibition and the part it plays in the normal activity of the cerebral cortex are illustrated and discussed. The next chapters are devoted to the analysing and synthesising activity of the cerebral hemispheres and to the irradiation and concentration of nervous processes in the cortex. This is followed by a discussion of the essential nature of cortical activity, and of the physiological properties of different parts of the cortex.

From this stage we are presented with a series of more specific problems. In the first place it is shown that, as far as their mechanisms go, sleep and internal inhibitions are the same process, and that when the inhibition does not spread to subcortical centres phenomena identical with those of hypnosis appear. We are here furnished for the first time with a physiological explanation of sleep, and an explanation which will fail to convince few who study these chapters carefully. The psychological hypotheses of sleep and hypnosis that have for long held the field can now be discarded. Other phenomena also which have been regarded as "psychological" receive physiological explanations based on controllable experiments; for instance "suggestion" in man is shown to be one of the simplest forms of conditioned reflex. His rigidly

scientific attitude forces the author to deny to psychology the right to be regarded as a science at all, in fact he insists there is no real line of demarcation between "nervous" and "psychic," the distinction is only arbitrary.

The last seven chapters have a closer relation to clinical neurology. Early in his study of conditioned reflexes Professor Pavlov observed functional disturbances of the nervous system in his experimental dogs which resemble, and are obviously closely allied to different types of neuroses met with in man, further investigations have shown that they are due to a conflict between the processes of excitation and inhibition, or to the action of extremely powerful stimuli, and have revealed the means by which they can be successfully treated. The effects of surgical lesions of the cortex on its normal activity as studied by the method of conditioned reflexes lead to an important discussion on the question of localization of function in the cortex, and the form that this localization takes, one conclusion is that his experiments emphatically refute the doctrine of special "association" centres, or of any special area on which the higher functions of the nervous system depend. The final chapter deals with the application of the experimental results to man.

It is impossible to review adequately in a limited space a volume which is not only stored with observations of an entirely new character, but which presents points of view with which few have been hitherto familiar. A mere list of its contents will, however, serve to show that its study is essential to all interested in any branch of neurology.

Travaux et Mémoires. Par Pierre Marie. Tome 2. Pp. 393. Paris : Masson et Cie. Price 30 francs.

The first volume of the reprints of his scientific articles which Professor Pierre Marie is issuing has been already noticed in this Journal. The second number contains a large number of short articles, some of which were published many years ago, others more recently, as well as a few of his longer and more important papers. Among these may be mentioned the original description by Charcot and Marie of "Peroneal Muscular Atrophy," which here appears under the title "Amyotrophie Charcot Marie"; his paper on "Hereditary Cerebellar Ataxy"; that on "Les Lacunaires," or pathological states distinguished by multiple small cavities in the brain; the pathology of Amyotrophic Lateral Sclerosis, and a discussion on the question of localization in the Internal Capsule.

This volume contains many articles which are still important from the pathological, as well as from the historical, point of view, and very few that offer no interest. An index would have made the two volumes more useful.

Beiträge zum Ticproblem. Von J. WILDER and J. SILBERMAN. S. 100. Berlin : S. Karger. 1927. Price M. 8.40.

A critical review of our present knowledge of the nature and pathogenesis of tics is certainly required. This monograph is a contribution to the subject,

but it can scarcely be claimed that it suffices our needs, for on the one hand it includes too many different conditions, as involuntary motor phenomena of organic origin as well as numerous functional or psychogenic disorders; while on the other its authors fail to analyse sufficiently the exact nature and mode of origin of some of the conditions with which they deal. There is, however, an adequate review of the literature on tics, and many interesting points are brought out, especially in the discussion on so-called functional tics, in the study of which they employed a modified form of psycho-analysis. In places there is a tendency to too much theorizing, as in the assumption that mental and emotional activities of relatively high levels are associated with the activity of the corpus striatum, a hypothesis they make to explain the frequent psychical disturbances that accompany tics of striatal origin. The second part of the monograph consists of the case histories and analyses of a large number of patients observed by the authors

Nerve Tracts of the Brain and Cord. By W. KEILLER. Pp. 456. New York: The Macmillan Company. 1927.

New textbooks on the anatomy of the nervous system appear year by year; some are written from the purely academic standpoint, while others are little more than introductions to elementary neurology. The author of this book professes his aim to be to enable students to study nervous diseases in terms of anatomy, physiology and pathology, and he has certainly produced a work which, if too detailed and voluminous for the ordinary student, will be of considerable use to the post-graduate worker.

In the first section of the book the central nervous system is studied in a series of sections, which are well represented by drawings, first as they are seen by the naked eye and then under the microscope. Owing to this arrangement there is a certain amount of repetition, which, though possibly advantageous in the classroom, adds unnecessarily to the size of the volume. The frequent references to the functions of the structures described will stimulate the student's interest.

In the second section, the motor, sensory, cerebellar and other systems are treated separately, and the functional significance of the different parts of each are discussed. A large part of this section is consequently physiological, and in it the author is on less sure ground and not so up to date as in the anatomical descriptions. The third section on, "Applied Neurology," attempts to explain clinical symptoms in terms of the functions of the parts involved by the lesions that produce them.

Almost all the illustrations are collected at the end of the book; many of them are not original, but the author has shown considerable discrimination in their choice. Unfortunately some of these, as well as his own drawings and diagrams, are reproduced on such a small scale as to diminish their value seriously.

Nasal Neurology, Headaches and Eye Disorders. By G. SLUDER. Pp. 428 with 167 illustrations. London: H. Kimpton. 1927. Price 50s.

The greater part of this book has no interest for the neurologist, while in the sections that deal with symptoms of nervous origin he will find many statements with which he cannot agree, and hypotheses that will astonish him. Several syndromes are described: (1) Vacuum frontal headache associated with eye-strain, the latter being explained by the attachment of the tendon of the superior oblique muscle to the wall of the frontal sinus. (2) Anterior ethmoidal or naso-ciliary neuralgia, characterized by pain in the forehead, between the eyes and along the nasal bones; it is due to a neuritis of the anterior ethmoidal nerve which lies superficial as it enters the nose and is therefore easily involved. (3) Nasal ganglion neuroses, due to the spread of inflammation or of toxins to Meckel's ganglion, which lies in closer relation to the nose than is generally believed. This may take the form of "lower half headache," or pain spreading from the nose and orbits along the base of the skull to the mastoids, occipital region and shoulders; or the "sympathetic syndrome" consisting of vasomotor and secretory phenomena, "very wide in distribution and wondrously complex," and asthma. (4) Sphenoiditis associated with inflammatory or toxic affections of the optic, ocular and trigeminal nerves.

Birth Injuries of the Central Nervous System. Part I: Cerebral Birth Injuries. By FRANK R. FORD. Part II: Cord Birth Injuries. By BRONSON CROTHERS and MARIAN C. PUTNAM. Medicine Monographs, Vol. XI. London: Baillière Tindall and Cox. 1927.

In Part I of this most interesting work the author attempts a survey of the vexed question of the relationship of birth injuries to the subsequent development of nervous disease. His personal material has been gleaned from an analysis of 200 cases of bilateral spastic paralysis. The literature of the subject has been well investigated and is given in a useful bibliography. The author's conclusions are avowedly imperfect and partake more of the nature of a series of impressions. There is, however, very convincing evidence that the congenital diplegias, which constitute by far the largest group of infantile spastic palsies, are not to be attributable to meningeal hæmorrhage at birth, but are the result of various pathological processes of intra-uterine origin. No final statement could be made as to the relation of intracranial birth injury and chronic hydrocephalus.

The common diffuse meningeal hæmorrhage which is not large enough to cause death apparently leaves no residuum in the overwhelming majority of cases. The true traumatic cerebral birth palsies are represented clinically by the hemiplegias, the monoplegias, and the asymmetrical and unequal bilateral spastic paralysees, and have for their pathological basis intracerebral hæmo-

rhages, depressed fractures with laceration of the brain, and encapsulated meningeal hæmatomata. Such a clinical group do not amount to more than 6 per cent. of all infantile cerebral palsies. This monograph demonstrates clearly the present lack of accurate neurological investigation and classification based upon large series of cases of infantile spastic paralysis, secondly, it demonstrates the necessity for an investigation of the subsequent fate of a series of known non-fatal birth injuries, the obstetrical and early clinical data being available.

Part II. The second half of the volume deals with birth injuries of the spinal cord. The authors are to be congratulated in collecting a remarkable series of twenty-eight such cases. By the publication of these and analogous cases gleaned from the scattered literature, they have pointed the way to a veritable *terra incognita* of neurology.

Traction on the after-coming head has been the chief factor responsible for these injuries, which apparently vary not only in severity and distribution, but also in their ultimate outlook. Although no pathological evidence is forthcoming in the personal series of cases, it appears from the accounts of other published cases that all degrees of damage to the cord may occur—localized or diffuse—with or without lesions in the meninges or vertebral column, up to complete trans-section. The difficult task of physical examination has been carried out by the authors according to the "methods of the physiological laboratory," which are apparently synonymous with those of an incomplete neurological examination. In view of the peculiar value of the clinical cases, it is unfortunate that the authors did not obtain the co-operation of a neurologist.

Convulsions et épilepsie des enfants. Par ANDRÉ COLLIN. Paris : Doin and Cie. 1926.

In the first section the author deals with the greater aptitude of the young towards the convulsive state, and three lines of argument are pursued—histological, chemical, and hormonal. Incomplete insulation of the immature neurone is comparable with instances of pathological sclerosis occurring in the adult—both conditions being attended by an exaggerated convulsant aptitude. Instability of the calcium metabolism of the infant is the second predisposing factor, the third being the incomplete development of the antitoxin function of the endocrine system.

A clinical discussion follows upon the epileptoid states in infancy, distinction is made between benign convulsions occurring in the offspring of neuropathic parents as a result of peripheral irritation or intestinal disorders, and the fits of essential epilepsy commencing at an unusually early age. The points of differential diagnosis and the dissimilar prognostic significance are then considered.

The diagnosis of idiopathic epilepsy arising in the first decade is carefully considered by the author.

A hypothetical consideration of the mechanism of epilepsy is undertaken, and evidence is advanced to demonstrate a marked neurovegetative instability; such lack of equilibrium is regarded as the result rather than cause of cortical dysfunction. The prognosis of childhood epilepsy is markedly influenced, according to the author, by the onset of puberty, at this epoch many of the labile endocrine and metabolic factors become stabilized, often with permanent benefit to the convulsive state.

The monograph is concluded by a short chapter on treatment

Les ramollissements sylviens. Par MAURICE-LÉVY. Paris: Doin et Cie. 1927.

The untimely death of Charles Foix struck a profound blow to the French neurology, for he was the instigator of a new type of clinico-pathological approach to the subject of cerebro-vascular disease. By his elaborate and painstaking correlation of clinical phenomena with the finer macroscopic anatomical data, a new neurological chapter was being compiled on the subject of neuro-angiology. Fortunately, Foix had inspired a school of younger physicians who are continuing his work. The present monograph on the syndromes of the middle cerebral artery is a worthy contribution; it is an elaboration of a posthumous paper on the same subject by Foix and Levy, which recently appeared in the *Revue Neurologique*. The minute anatomy of the artery is first discussed and, in agreement with the work of Shellshear among British workers, it is shown that the branches are laid down with precision, and are constant in their distribution, abnormalities in the arterial arrangement consist in anomalies in the point of origin only, the ultimate destination is absolute. The course and distribution of the individual ramifications are described. Levy next deals with the symptomatology dependent upon occlusion of individual branches, and also of the main trunk at different levels. Thus one is led up to the conception of complete and incomplete Sylvian softenings. The latter may be superficial or deep (partial and complete); or they may be of the nature of a partial or total "posterior" occlusion. Syndromes dependent upon lesions of individual arteries are next described, and the question of bilateral and multiple softenings is approached. Throughout the work the dictum of Foix is stressed, that in cases of partial or complete arterial obliteration the most ischaemic zone is that most proximal to the point of obstruction, while the more distal areas are relatively immune. The latter half of the book is occupied by records of illustrative cases—numbering forty-five in all—most of which occurred in the author's own practice.

Post-Encephalitic Respiratory Disorders. By SMITH ELY JELLIFFE. Nervous and Mental Disease Monograph Series, No. 45. New York and Washington. 1927.

The first part of this monograph is historical in scope and gives a valuable and detailed analysis of the numerous cases of respiratory disorder recorded to date. Full descriptions of the author's two cases follow, and details are given

of a psycho-analytical investigation. Case 1 lost all respiratory symptoms whilst under treatment; the outcome in Case 2 is not reported. The third and fourth sections of the work deal with phenomenology and psychopathological problems. The author has, in company with Runge and Witzel, emphasized the psychological factors at work in these patients and believes that the "encephalitic cases are doing the best they can with those pathways which are left open for functioning." This monograph is of interest, but contains much that will be unacceptable to present neurological thought. In places the argument is so vague as to be incomprehensible, and the writing savours more of mysticism than of medicine.

Les nouvelles méthodes sur les réactions colloïdales du liquide céphalo-rachidien. Par EUGÈNE DE THURZO. Paris: Maloine. 1927. Pp. 180. Price 30 fr.

The first part of this monograph is occupied by a consideration of the author's modification of the colloidal benzoin reaction. By the addition of "licht-grün" and fuchsin to the alcoholic solution of benzoin, a "bicolour" component is added to the ordinary precipitation test of Guillain. The author emphasizes the delicacy of the reaction in neurosyphilis. A colour modification of the colloidal mastic test is also detailed. A series of spinal fluid examinations was carried out, using Kafka's colloidal paraffin; the simplicity of this last test is commented upon, but a relative slowness in precipitation and the greater element of subjectivity in reading the tubes are points of disadvantage. The latter half of the book deals with the behaviour of the colloidal reactions in neurosyphilitic fluids after treatment, in disseminated sclerosis and encephalitis, and after artificial inflation of the ventricles with air. The varieties of colloidal shellac reactions are considered finally.

Les tumeurs de la moelle. Par J. A. CHAVANAY. Pp. 78. Paris: Doyn et Cie. 1928.

This is a concise and interesting little résumé of the clinical manifestations of spinal cord tumours. The pathological and physiological aspects are not dealt with; the symptomatology is given in a clear and unequivocal manner, though many well-known features of a clinical nature are not mentioned. There is a chapter dealing with the spinal fluid changes, with the results of monometric studies, and with the injection of air or lipiodol into the subarachnoid space. The indications and results of surgical intervention are considered, and treatment by X-rays is referred to briefly. A short bibliography concludes the volume.

Anatomical, Phylogenetical and Clinical Studies on the Central Nervous System By B. BROUWER. Baltimore: The Williams and Wilkins Co. 1927.

Within this volume are contained the ten lectures delivered by Professor Brouwer at the University of Johns Hopkins, and are set out in the author's

usual lucid and naive style the views upon many of the problems of neurology which are associated so closely with his name.

The first lecture deals with the projection of the retina on the brain; by means of a method of experimental ablation of special sectors of the retina, the secondary degenerations were traced by the Marchi method as far as the lateral geniculate body in a series of cats, rabbits, and monkeys. Brouwer's conclusions lend support mainly to the localization theories of Henschen; he finds that in the chiasma the fibres from the upper part of the retina cross dorsally, while the macular fibres lie chiefly in the middle. This clear-cut localization is recognizable, moreover, in the primary optic centres, and it is pointed out that as one passes from an oral to a caudal direction, the representation of the macula becomes relatively greater in area. Brouwer's conclusions concerning the cortical representation of the retina are not yet mature, but his impressions are that as regards the projection for binocular vision, the idea of an exact localization must be given the lead; furthermore, the projection of the macula must be localized, but nevertheless over a wide area—in this way supporting the view of Holmes. Throughout this work the author stresses the importance of localization in three dimensional planes.

Lecture 2 considers the pathology of sensibility, Brouwer approaches the subject from a biological aspect and deals with "gnostic" as opposed to "vital" sensibility. The former is subserved anatomically by the tracts in the posterior column, the mesial fillet, and the radiations between thalamus and post-central cortex. The pathways for transmission of vital sensibility are more complex, and the central representation is widespread and diffuse; the centripetal fibres of the automatic nervous system probably take part. By a series of comparative anatomical studies it is shown that the vital sensibility is the more primitive variety and must be localized to the antero-lateral columns; gnostic sensibility is the neotype, and does not appear in the phylogenetic scale until the amphibians, reptiles, or birds; it is of later development in the human foetus. This form of sensation is localized to the posterior columns.

The last lecture concerns the significance of phylogenetic studies for the neurologist. The first example chosen is of a case of localized cerebellar atrophy occurring in an adult, and the light thrown by it upon the problem of cerebellar segmentation. Brouwer is led to agree in the main with Edinger's conception of neo- and palæo-cerebellum, the olivary system, too, appears as a duplicate structure, the accessory olives and the oral portion of the principal olive belonging to the palæo-cerebellar system, and the remainder to the neo-cerebellum. The author next takes the phenomenology of disseminated sclerosis as an illustration of diffuse lesions occurring haphazard throughout the central nervous system, but producing symptoms only in accordance with the principles of evolution and dissolution. The clinical results of such lesions are in the main the product of disorder of the newest and most highly evolved functions. Hence one finds rigidity of the abdominal responses, rather than of the knee-jerks; inco-ordination and spasticity rather than paralysis; speech disorders before cranial nerve disorders; and nystagmus.

Idiosyncrasies. By Sir HUMPHRY RILEY. London: Kegan Paul, Trench, Trübner and Co. 1927. Price 2s. 6d.

This little book, one of the *Psyche Miscellany Medical Series*, is a most useful compendium of a subject which, though it is little understood, has a vast literature. The subject is discussed in the pleasantly worded, scholarly manner which one associates with the author.

The book is worth reading for the introduction alone; it would tax most people lucidly to define the term "idiosyncrasy." The sections on physiological hypersensitiveness, food and drug idiosyncrasies, and asthma, will be particularly useful, both to the practitioner and the student. Those who wish to study the subjects more extensively will find references to the literature quoted.

Psychologies of 1925. Edited by CARL LERHSON. Clark University, Mass. 2nd Edition. Oxford: University Press. 1927. 28s net.

In a comparatively brief space each of the outstanding figures in modern psychology gives a résumé of his point of view. The volume is divided into six parts, each devoted to a definite psychological approach.

Part 1 concerns "Behaviourism," and is written mainly by Dr. Watson, its protagonist, and by W. S. Hunter. In "What the Nursery says about our Instincts," and "The Experimental Studies on the Growth of the Emotions," Watson again propounds the physiological standpoint which is tantamount to a complete denial of the autonomy of psychology, and the familiar psychological views of instinct.

In Part 2, Robert S. Woodworth explains his "Dynamic Psychology," which denies the validity of "Behaviourism" and asserts the agency of mind as a dynamic force, but does not leave the realm of biology, as many psychologists do.

Part 3 is devoted to the "Gestalt" psychology and here its two great exponents, Koffka and Kohler, deal with mental development and the intelligence of apes respectively. The theory of "Gestalt" has little use for behaviourism, although it accepts its experimental methods. Here mind reasserts itself fully, and the theory expounds, on the basis of considerable experimental research, the way in which the external world is apprehended as a system of configurations which mind imposes upon it.

Part 4, "The Purposive Groups" expresses the errors of behaviourism, deals with the dynamics of co-consciousness and multiple personality, and a denial of the mechanical theory of man's mental life. These chapters are contributed by Morton Prince and McDougal.

Part 5 is concerned with "Reaction Psychology" by Knight Dunlap, and

Part 6, "Psychologies called Structural," by Harrison Bentley.

Although there are striking divergencies of view in this volume of surveys, one welcome feature is outstanding and admitted by all writers, that is, the insistence on biological categories in the treatment of all psychological problems.

Zwang und Zweifel. Teil 1. By WILHELM STEKEL. Wien: Urban und Schwarzenberg. P. 633. 1927. Price M. 30.

This volume is the first part of the ninth volume of Stekel's collected works: "Störungen des Trieb und Affektlebens."

In this enormous volume he deals with the nature and psychotherapy of Compulsion and Doubts. He classifies compulsive neuroses according as they arise from some anxiety about the organs (principally sexual), as result of education, and lastly because of the Ego demands. He distinguishes psychopathic doubt from philosophic doubt or scepticism; for him it is merely a symptom of deeper affective disturbances. The book is more or less free of any systematic attack on psychological problems, and from his copious case-histories and his discoveries, it is obvious that he manages to achieve understanding and cure without reference to the Unconscious or any other Freudian mechanism. But he never hesitates to take the cream of other people's discoveries and apply them with a hearty optimism, which is very amusing and frequently instructive.

Das autistisch-undisziplinierte Denken in der Medizin und seine Überwindung. By E. BLEULER. Berlin: Julius Springer. 1927. 4th Edition. Price M. 7.50.

This edition differs from its predecessors only in the addition of some important footnotes to the text. The book deals with the general character of Autistic Thinking, that is, that type of mental activity which goes on independent of reference to external reality. To this extent it is undisciplined, i.e., ungoverned by the logical demands of external reality. It must, Bleuler says, be sharply distinguished from "egoistic" thinking which is subject to the discipline of the organized Ego.

The volume is full of interest not only to the psychiatrist but for the general physician. The book is illuminated throughout by that calm wisdom which has always been expected and given in the writings of Bleuler, perhaps the sanest of living psychiatrists.

Études sur la circulation de l'influx nerveux dans l'arc réflexe. By A. RADOVICI. Préface de G. BOURGUIGNON. Paris: Masson et Cie. Price 16 francs.

Dr. Radović's monograph is an experimental investigation of the application of the chronaxic theory of Lapicque to human nerve physiology. It demonstrates the possibility of extending the theory from neuro-muscular phenomena, in particular as worked out by Lapicque and Bourguignon, to intraneural excitation of the axon itself. His researches establish definitely the rôle of the "time" factor in all laws governing the relationship between stimulus and response. In experiments made on man with the cord "released" by compression lesions, it is demonstrated that the automatic and rhythmic

reflex movements in the limbs below the lesion have a frequency varying according to a definite law, corresponding also with the frequency of the electrical stimulation. The law is identical with Weber's law of sensation, Pfeiffer's tropism phenomena, and with Hedwig's observations on embryonic development. His observations are also found to agree with Lehman's work on the retina, and Waller's on the optic nerve.

Weber's law of the relation between stimulus and sensation, in other words, is nothing else than a purely neurological law, and psycho-physical parallelism becomes in consequence electro-physical parallelism.

Beiträge zur Kenntnis der mongoloiden Missbildung. By M. W. M. van der SCHEER. Berlin. S. Karger. 1927. Price M 12.

This monograph is a statistical, anatomical and clinical investigation of the part played by the uterine mucous membrane and the amnion in the production of the deformity known as mongolism.

The study is a very thorough one and the subject of definition of terms is carefully considered. The first section deals with general considerations and the anthropological arguments are discussed, and an interesting compromise is suggested between Crookshank's purely racial explanation and the embryological aetiology of the condition. It is the latter which concerns the author, and he deals statistically and clinically with the affections of the uterine mucosa which may cause the deformities. The third section discusses the specific somatic and psychical features of mongolism.

The monograph is useful because all aetiological factors are considered and the differential diagnosis from mental deficiency is constantly being borne in mind.

The Psychology of Murder. A Study in Criminal Psychology. By A. BJERRE. Longmans, Green and Co., Ltd. 1927. 9s net.

Bjerre occupied an important position in the Danish judicature and had ample opportunity of studying the details of each of the cases with which he deals. Although he is of the opinion that the cases he had under investigation were capable of classification under three heads—self-deception, anguished fear, and shamming, he has noted common qualities binding all clinical manifestations together, namely, psychological emptiness and a tendency towards general mental weakness. In each case a very full account has been given of the crime which brought each delinquent to justice, and the background of the crime is carefully looked into. However this may be, the author treats throughout of the superficial mechanisms that actuated the crime, and of the essential weakness exhibited in facing environment, and in so concentrating his attention he has lost the inwardness of the whole criminal psychology. The unconscious promptings of crime, the deep compensatory mechanisms, are missed and are merely dealt with as if the conversations were done deliberately.

in order to gain easier ends. These criticisms while diminishing the scientific value of the book do not detract from its practical use. The book remains an interesting contribution to criminology, particularly as the author opens up the avenue to the pathological approach as against the legal approach to the study of crime.

Selected Papers on Psycho-Analysis. By KARL ABRAHAMS. International Library of Psycho-Analysis. No. 13. London: Hogarth Press. 1927. Price 30s.

This volume is in the nature of a memorial to the late Karl Abrahams, who was perhaps, after Freud, the outstanding pioneer of psycho-analysis. It is a collection of all the writings he contributed on the subject, and illustrates the many-sidedness of his work, and this renders it impossible in a short review to deal adequately with the mine of information he has worked so assiduously. Firstly, it illustrates his pre-occupation with the evolution of the child-mind, and the contribution that the affective life of the child makes to adult psychology. Secondly, it shows his interest in the psychoses and the light that psycho-analysis attempts to throw on their development. Thirdly, his wide cultured interests and linguistic powers are manifest in his researches into applied psychology, that is, psycho-analysis applied to folklore, history and education.

Dr. Ernest Jones gives an interesting memoir of the author and schematizes his positive contribution to the subject and his application of Freud's doctrines

- (1) *Correlated Physiological and Morphological Studies of the Development of Electrically Responsive Areas in the Cerebral Cortex of the Opossum.* (2) *Histological Development of Cerebral Motor Areas in Young Kittens correlated with their Physiological Reaction to Electrical Stimulation.* By ORTHELLO R. LANGWORTHY. "Contributions to Embryology," Nos. 103 and 104. Reprinted from Vol. xix of "Contributions to Embryology." Carnegie Institute, Washington. Publication No. 380. 1927. Pp. 149 and 177.

In these studies the author has used the pouch-young of the opossum and newly-born kittens in order to determine the order in which the motor areas for the various segments of the body become differentiated and electrically excitable. By using the pouch-young of Virginian opossums he obtained what were practically air-breathing embryos, as these animals are born when only 11 mm. in length. They appear to climb up into the pouch by grasping the hair with their fore-limbs, and in accordance with this the author found that the fore-limb centre was the first to become differentiated and electrically excitable. No area which produced movements of the hind-limbs was discovered by him, even in adult opossums. In this his findings agree with those

of Cunningham. In the kitten also the area for the fore-limb was excitable at birth, and this was followed by the area for the hind-limb at 16 days, and the area for the face at 21 days. These dates corresponded with the state of maturity of the cortex and not with the myelination of the pyramidal tract, as this is not myelinated at all till the age of 9 or 10 days.

Certain other points, such as the development of Brodmann's *area frontalis agranularis*, were also brought out by these experiments.

Zellaufbau der Grosshirnrinde des Menschen. By Dr. CONSTANTIN VON ECONOMO. S. 146. Berlin: Julius Springer. 1927. Price 18 marks.

L'architecture cellulaire normale de l'écorce cérébrale. French edition, translated by Dr. LUDO VAN BOGAERT. Pp. 183. Paris: Masson et Cie. 1927. Price 80 francs.

The author prefaces this work by the explanation that it is not meant to replace his large atlas, but rather to form an introduction to it. In any case it is of itself a very useful book, as it presents the detailed cell structure of the cerebral cortex in an easily assimilable form. The 109 types of cortex are grouped into five main-forms which are probably functionally as well as histologically distinct. By his system of naming each of the cortical areas by a letter-group, the author preserves the gross anatomical nomenclature, and at the same time gives an indication of the type of cortex present in each area. This system seems to us a definite improvement on the numerical system of Brodmann, although, whether as a result of it, or for other reasons, the number of different cortical areas is more than doubled.

The book is beautifully illustrated, and the forty large photomicrographs of the most distinctive cortical areas make it a book which will be as useful for reference in the laboratory as for home study. The French translation by Dr. Ludo van Bogaert has been well done, and the use of headlines in it of headlines to the paragraphs in leaded type facilitates reference. Both volumes are most welcome additions to the neurologist's library.

Embryology of the Neuromuscular Spindle. By FIDEL CUAJUNCO. "Contributions to Embryology," No. 99. Carnegie Institute, Washington. Publication No. 380. 1927.

This small monograph is a record of an investigation into the development of the neuromuscular spindle and of its nerve-supply in pig embryos. The author confirms the classical researches of Sherrington and of Batten in finding the spindles supplied with sensory and not with motor nerve-endings, but he also found some twigs which appeared to be of sympathetic origin terminating within the capsule. It is interesting to note that the nerve-supply reaches the embryonic muscle fibres before they become segregated off by the capsule of the spindle.

The illustrations are excellent, but in those of the complex nerve-endings it is not always clear how much is photomicrograph and how much drawing. Undoubtedly good drawings illustrate the author's intentions better than the best photomicrographs, and a little touching up of photographs is excusable, but this does not altogether exculpate the author from describing as a photomicrograph what appears to be, as far as the more important details are concerned, the result of pen and ink.

Die Lagereflexe beim Menschen. By HANS HOFF und PAUL SCHILDER.
S. 182. Wien: J. Springer. 1927. Price 12 marks.

The authors have defined their book as an account of the attempt to apply to the clinical material at the Vienna clinic those principles of posture regulation laid down by Magnus in his work on "Körperstellung." It contains firstly a very complete and up-to-date summary of the reflexes worked out in the school at Utrecht. Following this, there is a further summary of the anatomy of those tracts and central nervous mechanisms, particularly of the red nucleus and its connections, which are held to supply the machinery for these reactions.

The main body of their book is concerned with observations on the postural reflexes in adults, but is preceded by a shorter account of those already described in the normal infant by Minkowski, Gamper, Schaltenbrand and others, and their contribution to this part of the subject consists in a very useful résumé of the appearance and disappearance of these reflexes as age advances.

With those reflexes which appear in premature infants, or those with various forms of cerebral age or trauma, they are less concerned, although these form an interesting comparative link between the experimental animal and the normal child.

It appears from the observations that the transition of reflex activity from the condition of the infant at birth to that of the normal adult may be divided conveniently into four periods. The first lasts from birth to 6 months, during which the reactions to movement (Bewegungsreaktionen) are prominent; the next a quadruplegic condition, in which the characteristic primitive postural reflexes, as described in animals, are to be seen, the third, in which the tonic influences which determine the quadruplegic position gradually diminish, with the assumption of the erect attitude, and the final stage, complete by the fifth year, in which the postural reflexes have assumed a form which they maintain throughout adult life.

The authors have elaborated a series of clinical tests which are clearly and practically detailed, and of which the normal variations in response are precisely given. The results of the application of these tests to patients suffering from a variety of nervous lesions, especially lesions of the cerebellum, provide the material for most of the rest of the book which closes with a tabular summary of the chief results therein detailed.

It is clear that many reactions in man find no counterpart in the behaviour of experimental animals, and that only by analogy can their mechanism be localized with any degree of probability within the mid-brain. Many of these have, however, been shown to yield definite localizing value as clinical tests on purely empirical grounds.

The authors have taken great care in their attempt to decide how far the defect which accounts for the appearance of such reactions is sensory or motor in nature, and herein lies the chief basis for criticism of this work, in that, as they would readily themselves admit, this discrimination is seldom possible with certainty, and indeed, in some cases the defect may be in part neither sensory nor motor, but definitely perceptual as in the Lagebeharrungsversuch and the Imitationsphanomen.

This detracts in no wise from the very considerable value of the book as a whole, and the detailed bibliography at the end is admirably complete and clear.

Les réflexes de posture élémentaires. Par P. DELMAS MARSALET.
Pp. 176. Paris: Masson et Cie. 1927. Price 16 francs.

In this book Marsalet has recounted his investigations of the clinical occurrence described by Foix and Thevenard, which consists in the shortening of a muscle secondary to its passive relaxation, such shortening being, in their opinion, a response on the part of the muscle designed to fix it "without slack" at the newly-imposed length. Working with the tibialis anticus muscle, the procedure of Delmas Marsalet has been to approximate its origin and insertion passively and quickly by sudden dorsiflexion and inversion of the ankle, and by means of a tambour fixed over the subcutaneous portion of its tendon, where it bridges over the ankle, to record the subsequent readjustment of tension by active contraction of the muscle.

He has found abolition of this reflex in polyneuritis, tabes, flaccid hemiplegia and cerebellar hypotonia; its replacement by an intermittent clonic response, in cases of damage of the pyramidal tract, and its exaggeration in cases of Parkinsonism. He then proceeds to describe the various factors which can be used to modify at will the reflex examined; continued passive movements of the limb which transitorily diminish the reflex and various drugs, the most prominent of which was scopolamine, which abolish it when in sufficient (1.25 mgm.) doses after an interval of three-quarters of an hour.

He has come to the conclusion that the reflex is a widespread one, involving many nervous pathways, and that its nervous mechanism is quite other than that of the tendon reflexes. He finds further that in cases of Parkinsonism there is a strict correspondence between the distribution of the rigidity and the occurrence of exaggeration of the postural reflexes—a correspondence which is both topographical and proportional in degree, so that he is led to ascribe a causal relationship to the two phenomena, and states that all the characteristic features of this condition dependent upon rigidity are due to the exaggeration of the postural reflexes.

Unfortunately there is no serious attempt to substantiate the hypothesis that this phenomena is reflex and no evidence that the explanation offered is the correct or even the most probable one.

The interpretation of this reaction in the terms of the physiology of nervous reflexes is seriously open to question, and it is a pity that this type of response should be described as a postural reflex when this term has been already used to describe the series of delicately adapted reaction so ably and scientifically investigated by Magnus and his workers, and to which this bears no relation whatever.

J. HUGHLINGS JACKSON: *Ueber Aufbau und Abbau des Nervensystems*.
Uebersetzt und eingeleitet von OTTO SITTIG. S. 137. Berlin:
S. Karger. 1927. Price 6.60 marks.

Sittig's translation into German of Hughlings Jackson's "A Study of Convulsions," has been already noticed in this Journal. He has now translated Jackson's "Croonian Lectures," which is one of his most important articles, and contains some of the most valuable contributions he made to the study of the nervous system in health and disease.

As on the previous occasion, the English text and the German translation appear on opposite pages; the value of this to everyone to whom English is a foreign tongue is obvious, and fortunately it also makes available to English readers these lectures which have never been reprinted since they originally appeared in the *Lancet*. The translation seems to be accurate and readable.

Epidemic Encephalitis. By L. M. CRAFTS. Pp. 237. Boston: R. E. Badger. 1927.

This volume is based on the author's own experience, but it also contains references to the literature of epidemic encephalitis. It presents concisely the main clinical features of this polymorphous disease, and discusses its differential diagnosis in considerable detail. Half its pages are devoted to case reports, most of which will be of use only to the student unfamiliar with its ordinary symptoms.

Kompendium der topischen Gehirn und Rückenmarksdiagnostik. Von R. BING. 7te Auflage. S. 259. Berlin: Urban und Schwarzenberg. 1927. Price 10 marks.

The successive editions of Bing's well-known textbook on the diagnosis of local lesions of the nervous system have been noticed in this Journal. The seventh edition has grown but little in bulk, but both the text and illustrations have been revised. The chief alterations have been made in the sections on the cerebellum, the basal ganglia and the visual system, but fuller reference will be found here to the postural reflexes and spinal automatism, subjects in which more exact knowledge has been recently acquired. The book remains one of the best of its scope available to the student of organic neurology.

Der Tonus der Skelettmuskulatur. Von E. A. SPIEGEL. 2te Auflage. S. 203. Berlin: J. Springer. 1927. Price 18 marks.

The first edition of this monograph, which appeared under the title, "Zur Physiologie und Pathologie des Skelettmuskeltonus," has been already reviewed (*Brain*, 1924, 47, 257). This, the second edition, is almost double its size, and contains much new matter as well as amplifications of many of the original sections. The further development has been chiefly in the direction of investigation of the nature muscle tone by animal experiments, and little reference is made to the clinical applications of the results obtained. The chief conclusions are that (1) In the labyrinthine nuclei and in the formatio reticularis of the hind-brain are supraspinal centres for extensor or antigravity tone, (2) the red nucleus is a centre which acts by inhibiting extensor tone, or by regulating the distribution of tone between the flexors and extensors; (3) the basal ganglia contains a reflex apparatus which can modify the relative tone of agonists and antagonists; (4) the cortico-spinal and cortico-pontine systems tend to inhibit extensor tone, (5) the cerebellum is a proprioceptive reflex mechanism which, on the one hand, acts as a brake, on the other diminishes the tone of the extensors and increases that of the flexors. (6) The autonomic nervous system has no influence on tone. These conclusions serve to indicate the importance of this monograph for all interested in the question of muscle tone, a subject that is daily taking a larger part in clinical neurology.

Mikroskopisch-topographischer Atlas des menschlichen Zentralnervensystems mit begleitendem Texte. Von O. MARBURG. 3te Auflage. S. 226. With 40 Illustrations in Text and 32 Tables. Wien: F. Deuticke. 1927. Price 28 marks.

It is now twenty-five years since the first edition of Marburg's Atlas appeared, and nearly twenty years since the second was published. The third edition is considerably enlarged, especially the descriptive pages and the sections on the cellular architecture of the cerebral cortex, and many new illustrations are provided. The Atlas still retains its essential features; a large number of excellent and wonderfully reproduced drawings of sections in various planes of all levels of the central nervous system are given, and the text consists mainly in descriptions of the individual sections. This method of study of anatomy is perhaps essential for the beginner, but alone it unfortunately fails to present to the student the clear picture of the structural connections of different parts of the brain and cord which is required in the practice of neurology. All the illustrations are fully legended, and a table gives the name in German, French, English and Italian of each structure indicated. In this table the figure in which tract or nucleus can be seen is also shown, so that anyone who is interested in any structure, as for instance, the acoustic radiation, can at once find its position and trace its course in the illustrations.

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EDITOR.

[JUNE, 1928.]

BRAIN.

PART 2, VOL. 51.

LIPODYSTROPHIES: REPORT OF SEVEN CASES.¹

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MORGAGNI probably recorded the earliest description of a case of progressive lipodystrophy. In the last half of the nineteenth century persons were seen who had lost subcutaneous fat from one or both sides of the face. Osler observed a case of progressive Epodystrophy in 1895, but did not publish a record of it. In 1906 Barraquer published a detailed description of a case which he referred to as "atrophy of the cellulo-adipose tissues." In 1907 Campbell described a case as "disappearance, more or less complete, of the subcutaneous fat above the region of the lower extremities." Other writers [22] reported cases, and in 1911 Simons [23] described one and introduced the term "progressive lipodystrophy," used chiefly since then as a diagnostic term for the disease. He defined it as a symmetrical and progressive loss of subcutaneous fat over the face, neck, arms, thorax and abdomen, with relative abundance of subcutaneous fat over the hips and lower extremities.

Although more than seventy cases have been reported in the literature, the seven cases observed in the Mayo Clinic present certain new and interesting clinical variations.

REPORT OF CASES.

Case 1.—A man, aged 49, first came to the Mayo Clinic in October, 1924, complaining of weakness of four months' duration. His father had died from diabetes mellitus. The patient had had pneumonia at the age of 16. In 1910 he began to notice fatigue and even exhaustion in carrying on his work. He became nervous; the pulse was rapid; the eyes protruded, the right more than the left, and vision failed in the right eye rather suddenly. In January, 1911,

¹ Submitted for publication August 17, 1927.

he was confined to his bed, perspiring freely and vomiting at times. Tremor was marked. His weight declined to 90 lb. He remained in bed seven months, and it was during this time that the right side of the face wasted. In July the right lobe of the thyroid was injected three times with something unknown to the patient. Soon afterward he began to improve and gain in weight, but while fat returned to every other part of the body, it failed to do so on the right side of the face. He noticed at this time recession of the right eye. Similar recurring attacks of exophthalmic goitre made subtotal thyroidectomy necessary in August, 1917, and in January, 1922.

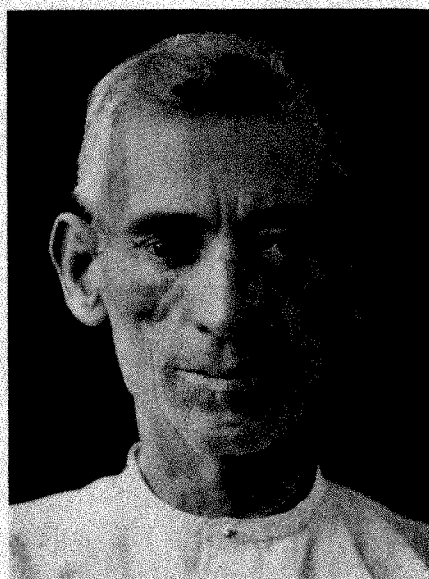


FIG. 1.—Case 1. Right facial hemiatrophy.

General examination.—The outstanding features in the examination were: Loss of weight (20 pounds below his usual weight); marked nervousness and restlessness; dental sepsis; large bilateral varicose veins; more than an average grade of arterio-sclerosis; atrophy of the right side of face and tongue; palpable thyroid gland without bruits; choroidal atrophy and degeneration in the right eye, and vitiligo (fig. 1).

Laboratory data and clinical course.—A trace of sugar was found in the urine, and two basal metabolic rates were +32 and +24. A consulting neurologist saw the patient and reported absence of subcutaneous fat in the right side of the face in the distribution of the fifth cranial nerve, and from the right side of the tongue, without loss of muscular power in these regions. A diagnosis of lipodystrophy facialis was made. The patient improved greatly on iodine (Lugol's solution), and decided to postpone thyroidectomy. Symptoms

recurred in March, 1925. The basal metabolic rate was +31, and the urine contained 2.42 per cent. sugar. The blood sugar was 0.13 per cent. The patient gained strength rapidly after subtotal thyroidectomy, and glycosuria disappeared by qualitative restriction of diet without the use of insulin. The pathologist reported "hypertrophic parenchymatous thyroid."

Comment.—Loss of subcutaneous fat from the right side of the face and tongue occurred at the age of 36 during the profound emaciation incident to the first of a series of recurring attacks of exophthalmic goitre. The hair, skin and muscles of the face had not been affected, but the distribution is suggestive of trophic nerve disturbance. The case might well be considered progressive facial hemiatrophy, which Stewart described as follows:—

"This disease, which commences in early life, usually before puberty and more often in females than in males, shows itself first in the skin of the face, either near the orbit or over the upper or lower jaw, gradually spreading over the whole face on one side. The skin becomes thinned from atrophy of the papillary layer, the subcutaneous fat disappears, and thus the affected side of the face becomes wrinkled and furrowed, in marked contrast with the healthy side. Later, the subjacent muscles, cartilages and bones become atrophied, but without motor paralysis or reaction of degeneration. The corresponding side of the tongue and occasionally that of the soft palate also become wasted. But the hemiatrophied tongue, when protruded, comes out straight, unlike that of a patient with atrophy from hypoglossal palsy. The hair on the affected side of the face may fall out or become white, and the sebaceous glands may atrophy. The scalp is rarely affected. There is no anæsthesia."

Recently Wolff and Ehrenclou reported the case of a woman with the onset, at the age of 32, of progressive facial hemiatrophy associated with progressive lipodystrophy. Cases have been reported in which fat atrophy began in one side of the face, later involving the other side, and ultimately progressing to typical progressive lipodystrophy. Husler reports bilateral fat atrophy of the face in two boys. Simons [24] was convinced that these were cases of progressive lipodystrophy.

Case 2.—A woman, aged 27, first came to the Mayo Clinic, February 12, 1925, complaining of swellings over the body of two years' duration, and marked weakness for more than three years. She had had whooping cough at the age of 4 and again at 13, measles some time during childhood, scarlatina at 15, tonsillitis occasionally, and influenza at 21. She said that she had never been strong. She had always been moderately constipated. There was no history of jaundice. At the age of 11 tender swellings, about 2 cm. in diameter,

appeared on the medial aspect of the thighs and lateral aspect of the legs below the knees. These disappeared in from two to three weeks, at which time all subcutaneous fat left the lower extremities, causing the muscles to stand out prominently. The muscles seemed hard to the touch, and when she walked her legs were noticeably stiff. At the age of 13 menses began after two months of hard coughing which was thought to be a second attack of pertussis. Menses were irregular (six weeks to six months apart) and the flow was moderate, but usually accompanied by epistaxis. At 16 she became very nervous and noted the development of a goitre. She was married at 22; at this time her face, arms, chest and abdomen were well covered with subcutaneous fat, but the lower extremities were lean, hard, and masculine in appearance. Soon after marriage she became pregnant; vomiting was frequent, and the pregnancy terminated in difficult labour (breech presentation). During pregnancy some brown spots appeared on the skin over the body, but there was no pruritus. Three months after the baby's birth she felt weak and her face became swollen and hard, and erysipelas was feared. The swelling was more pronounced in the morning, receding somewhat towards evening. The swelling persisted for three months, then disappeared gradually, and with it all subcutaneous fat in the upper part of the body. After the subcutaneous fat had disappeared from the upper part of the body, she noticed small nodular swellings along the sides of the neck, in the axillæ, in the breasts, and in the groin. These persisted approximately two months and then partially receded, at which time large, brownly pigmented itching areas appeared on the skin of the whole body. She complained of vague epigastric soreness, and it was then discovered that the spleen and liver were enlarged; they became huge within a few weeks; and during this time sugar was discovered in the urine, and she began to complain of polyuria and polydipsia.

General examination.—The outstanding features of the case were: Weakness, nervousness and dyspnoea; absence of subcutaneous fat over the whole body; muscles firm, giving the extremities a masculine appearance; brownish pigmented spots over the trunk, axillæ, and medial aspect of thighs; thyroid gland palpable but not enlarged; slight enlargement of lymph nodes of neck, groin and axillæ; huge, soft but not tender, liver, the notch of which came to the umbilicus; markedly enlarged spleen with lower edge at level of umbilicus, soft and compressible and not tender; enlargement of left kidney; systolic blood-pressure 155 and diastolic 95; pulse-rate 132, and temperature 99.2° F.

Laboratory data and clinical course.—A twelve-hour specimen of urine (950 c.c.) had a specific gravity 1.038; acid reaction; albumin graded 2 (on basis 1 to 4); sugar, 4.58 per cent.; acetone and diacetic acid, none; pus-cells, 7, to a low-power microscopic field. The hæmoglobin was 60 per cent.; the erythrocytes numbered 4,040,000, and the leucocytes 5,900; lymphocytes, 27.5 per cent.; large mononuclears, 5.0 per cent.; transitionals, 7.5 per cent.; neutrophils, 56.0 per cent.; eosinophils, 2.0 per cent.; basophils, 2.0 per cent.; slight anisocytosis and poikilocytosis; platelets, 116,000; Bogg's coagulation time, five minutes. Bleeding time, one and a half minutes. Blood Group II. In

the test for fragility of erythrocytes, hæmolysis of the cells of the patient began at 0.48 per cent. sodium chloride and was complete at 0.36 per cent., and hæmolysis of the cells of the control began at 0.44 per cent. and was complete at 0.32 per cent., thus suggestive of slight increase in fragility. The blood-sugar was 0.13 per cent., and the carbon dioxide combining power of the plasma was 54 per cent. The Wassermann test on the blood was negative. There was no retention of dye in tests of hepatic function; two estimations of serum bilirubin were 0.66 mg. and 0.50 mg. for each 100 c.c. The stools were not examined. Six basal metabolic rates, taken between February 20 and March 6, were +57, +48, +40, +44, +45, and +55, respectively. The lymph node removed was inflammatory. There was no evidence of fat-ingesting macrophages.

Consulting physicians found it difficult to explain the hepatomegaly and splenomegaly. The case resembled Hanot's hypertrophic biliary cirrhosis. The neurologist found no objective neurological disturbances, except total absence of subcutaneous fat. A diagnosis was made of progressive lipodystrophy. The dermatologist made a diagnosis of tinea versicolor and transitory benign plaques of the tongue.

Because of the persistently high basal metabolic rate, iodine was given without perceptible effect. The glycosuria was easily controlled by qualitative restriction in diet without insulin. Subtotal thyroidectomy was performed March 11, 1925. The pathologist's report was, "Colloid and foetal thyroid with extensive interacinar hyalinization." The liver and spleen receded only slightly following thyroidectomy, and the basal metabolic rates, March 21 and March 24, were +52 and +59 respectively. Unfortunately a photograph was not obtainable. From reports received within the last year, it would appear that the patient's condition has changed very little.

Comment.—This case presents at least three unusual features. The patient lost the subcutaneous fat from the lower extremities, then she lost it from the entire body in two fairly distinct attacks which appeared to be inflammatory, and finally the associated hepatomegaly, splenomegaly, adenopathy, diabetes mellitus, high basal metabolic rate, and skin manifestations formed a clinical picture the like of which I have been unable to find described in the literature.

Gilchrist and Ketron describe the case of a girl aged 8 years, whose subcutaneous fat disappeared from the lower extremities irregularly, so that the legs presented a nodular appearance similar to that in Case 2. They examined the skin and fatty tissue in their case in the active stage, and found large macrophages ingesting fat in large quantities. Bignami, cited by Zella, reported a case in which the fat disappeared in an irregular manner, leaving a nodular appearance of the body.

Case 3.—A woman, aged 31, came to the Mayo Clinic in August, 1922, complaining of "swelling of the legs" since the age of 16. Menstruation began at 12, and was regular until she had pneumonia at 16. Following the attack of pneumonia, during which she was in bed for three weeks, the cheeks became sunken and the legs and hips began to enlarge. Following the birth of her only child, at the age of 24, she had puerperal infection and was in bed three months. Symptoms of peritonitis were marked. Subsequently the legs and hips began to enlarge markedly, while the face and upper trunk became thinner. Standing and walking caused dull aching pain in the lower extremities, and the legs had become so large and heavy as to interfere seriously with walking. Attacks of pain in the right lower quadrant of the abdomen also appeared. She admitted being somewhat nervous and wept rather easily. Occasionally she had mild attacks of headache over the temples associated with vomiting.

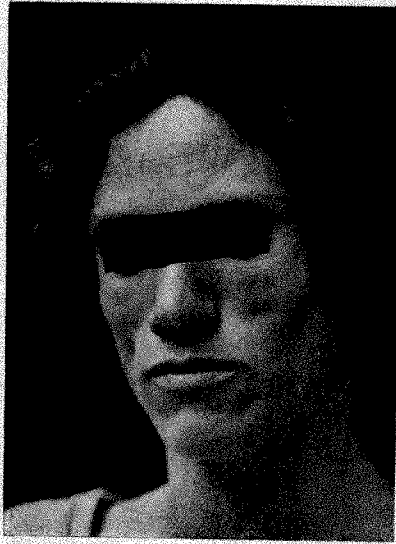


FIG. 2.—Case 3. Facies in progressive lipodystrophy.

General examination.—The chief features of the case were: Absence of subcutaneous fat down to Poupart's ligaments and the crests of the ilia, with huge deposits of subcutaneous fat below these levels; cartilaginous mass around the umbilicus, and dental sepsis (figs. 2 and 3).

Laboratory data and clinical course.—The urine contained a trace of albumin, but no sugar; it was normal microscopically. The hæmoglobin was 67 per cent.; erythrocytes numbered 4,340,000 and leucocytes 9,400; differential count of the leucocytes showed: lymphocytes, 36.5 per cent.; transitionals, 2.0 per cent.; large mononuclears, 0.5 per cent.; neutrophils, 55 per cent.; eosinophils, 4 per cent., and basophils, 2 per cent. The blood-sugar was 0.14

per cent. The Wassermann test on the blood was negative. The basal metabolic rate was +6. Roentgenograms of the head were negative.

Appendectomy was performed. The appendix was diseased, but other organs were essentially normal. The head of the pancreas was thought to be slightly enlarged. The patient was seen by a neurologist, who found no objective signs of disease of the central nervous system. A diagnosis of progressive lipodystrophy was made.

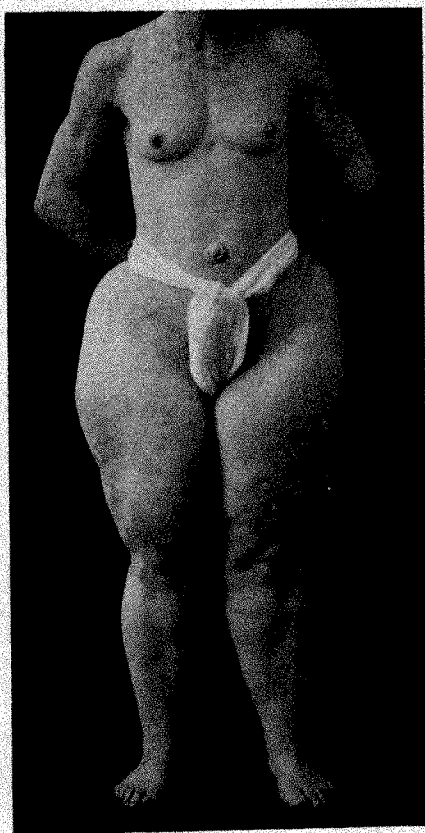


FIG. 3.—Case 3. Progressive lipodystrophy.

Comment.—This patient, with obvious difficulty in walking, presents the most typical aspects of progressive lipodystrophy of Simons that I have seen. The extreme increase in the size of the lower extremities suggested bilateral elephantiasis.

Case 4.—A woman, aged 42, came to the Mayo Clinic in March, 1927, complaining of general weakness of fifteen years' duration. All members of

her immediate family were well except her mother, whose ailment seemed obscure. The older of the patient's two children went blind from cataracts at the age of 2; he failed to develop mentally and had convulsive seizures. The patient's menses began at 14, and had been scanty but regular. At that time the patient had what was thought to be typhoid fever, after which she thought her cheeks never filled out. Up to the age of 27 she had never been strong, but was very ambitious and often became exhausted. She then suffered a nervous breakdown, characterized by weakness, mental depression, an oppressive feeling in the chest, and dyspnoea. Although she recovered from the acute manifestations of that breakdown, she failed to regain health and subsequently complained of many peculiar symptoms referable to the body. The

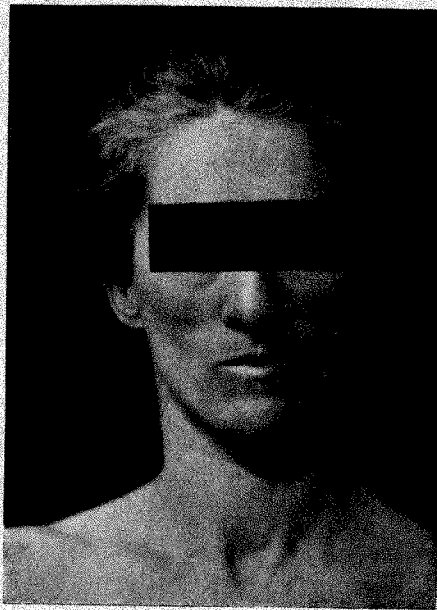


FIG. 4.—Case 4. Facies in progressive lipodystrophy.

nervous symptoms had so absorbed her attention that she gave little heed to the lipodystrophy, which had evidently begun at the age of 14.

General examination.—The chief features in the case were: Absence of subcutaneous fat down to the umbilicus, with increased fat over the hips; nervousness and tendency to dyspnoea; rectocele, cystocele, and lacerated cervix; systolic blood-pressure 134 and diastolic 94; pulse-rate 100; temperature, 99° F; palpable spleen, and moderately enlarged thyroid gland (figs. 4 and 5).

Laboratory data and clinical course.—The urine contained a trace of albumin but no sugar. The hæmoglobin was normal and cytologic examination of the blood negative. The sugar tolerance test was indefinite, but suggested

mild diabetes; at the beginning of the test the blood-sugar was 0.10 per cent., the volume of urine 140 c.c., and the urine did not contain sugar; 100 gm. of glucose was given, and after a half hour the blood-sugar was 0.165 per cent., the volume of urine 145 c.c., and the urine did not contain sugar; after two hours the blood-sugar was 0.124 per cent., the volume of urine 310 c.c., and there was a faint trace of sugar in the urine; after three hours the blood sugar was 0.116 per cent., the volume of urine 65 c.c., and the urine did not contain sugar. The Wassermann test on the blood was negative. The basal metabolic rate was +10. Roentgenograms showed the sella to be normal.



FIG. 5.—Case 4. Subcutaneous fat absent to the level of the umbilicus.

The neurologist's examination of the central nervous system was objectively negative, despite the multiplicity of complaints, the chief of which were weakness and "drawing sensations" in chest and abdomen. A diagnosis of progressive lipodystrophy with psychoneurotic reactions was made.

Comment.—This case presents in a mild way the typical manifestations of progressive lipodystrophy, with the onset at about the age of

14 after an attack thought to be typhoid fever. The chief features in this case were nervous symptoms of a psychoneurotic nature. Many of the complaints (tension, tight band) were confined to the region of the chest from which the fat had disappeared. Christiansen has observed psychical changes in the form of mental depression and anxiety associated with progressive lipodystrophy, and this, with other reasons, led him to believe that the disease is of nervous origin.

Case 5.—A woman, aged 22, came to the Mayo Clinic in July, 1926, because of loss of flesh from the face and upper part of the body, about which she was self-conscious. She had been brought to the Clinic in March, 1912, at the age of 8, because her parents had noticed that for the last two years her face had been growing thin. At this time she had epigastric pain immediately after eating, associated with frontal headache but unaccompanied by vomiting. She was nervous, and when under nervous strain her stools were loose. These symptoms persisted from childhood, although nervous symptoms had grown more pronounced. She had had tonsillitis and influenza, with good recovery. Menses had always been regular, but scanty.

General examination.—The chief features were: Absence of subcutaneous fat on the face, arms and trunk, the hips and legs being well developed and covered with a normal amount of subcutaneous fat; palpable thyroid gland; temperature 99° F; pulse-rate 80; systolic blood-pressure 138 and diastolic 86 (figs. 6 and 7).

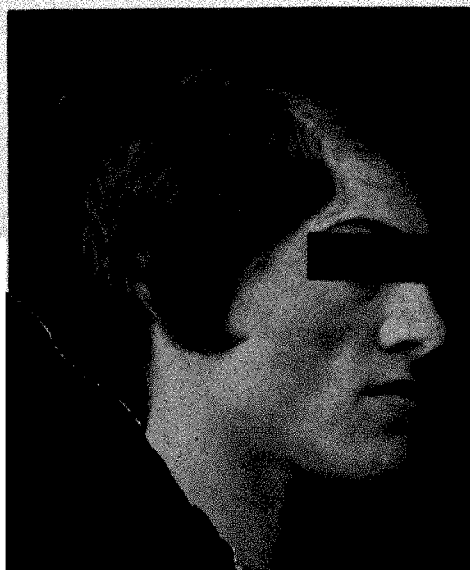
Laboratory data and clinical course.—A trace of albumin was found in the urine, but no sugar; it was normal microscopically. The hæmoglobin was 81 per cent.; the erythrocytes numbered 4,770,000, and the leucocytes numbered 12,000 at one time, and 13,000 and 14,000 at others; the differential count showed lymphocytes, 19.5 per cent.; transitionals, 1.0 per cent.; large mononuclears, 1.5 per cent.; neutrophils, 77.5 per cent., and basophils, 0.5 per cent. The Wassermann test on the blood was negative. Analysis of gastric contents showed total acidity 70 and free hydrochloric acid 50. *Endamoeba nana* were present in the stool. Roentgenograms of the sella turcica, chest, stomach, and colon were negative.

The neurologist found in the nervous system no objective signs of disease. A diagnosis was made of progressive lipodystrophy. The patient stated that she had been very nervous, chiefly because of her appearance, and had acquired a marked dislike for mirrors. She thought her physical endurance was above the average. She was again seen in April, 1927, at which time she seemed vigorous. She had taken whole pituitary without benefit. She had mastered her self-consciousness to a certain degree, and her endurance was excellent.

Comment.—This case is rather typical of progressive lipodystrophy: onset at the age of 6, accompanied by weakness, epigastric distress, and frontal headache. There was leucocytosis and the differential cell-

count was essentially normal. When the patient was under nervous tension the stools were loose.

Case 6.—A woman, aged 26, came to the Mayo Clinic in July, 1925, complaining of weakness of eight years' duration. The family history was unessential, except that her father had had hæmaturia. She had had tonsillitis as a child, and influenza at the age of 21. Since the beginning of menses, at the age of 13, with periods of amenorrhœa from September to December, she felt unusually strong and well. At the age of 18 she began to gain from 20 to 35 lb. during these periods. This fat was distributed over the hips and buttocks. In walking her weight tired her. During the remainder of the year, with the resumption of the menses, strength declined and menses were moderate and lasted five days.



test of the blood was negative. Cystoscopic examination was negative. The basal metabolic rate was -13 . Roentgenograms of the kidneys, spine and chest were negative.

The neurologist pronounced the objective examination of the nervous system to be negative.* He made a diagnosis of recurring lipodystrophy. The patient improved with the administration of ovarian extract three times a day. In the last year the period of amenorrhœa lasted only two months.

Comment.—This case is not typical of progressive lipodystrophy, but is of interest because of lipodystrophic changes associated with amenorrhœa. An endocrine cause for the disturbance might be considered.

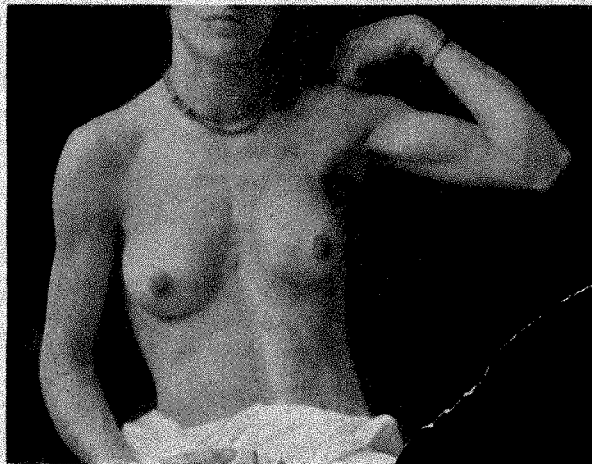


FIG. 7. —Case 5. Absence of subcutaneous fat causing

Case 7.—A man, aged 50, came to because of emaciation and loss of strength. Onset of diabetes mellitus less than one year. In 1911 and 1912 he had been afflicted with

General examination.—The chief features were: extreme emaciation; weight only 62·5 lb.; small nodular thyroid gland and perforated bilateral membrana tympani with foul-smelling discharge (fig. 8).

Laboratory data and clinical course.—A twenty-four hour specimen of urine (1,650 c.c.) showed a specific gravity of 1·034; acid reaction; no albumin; 130·6 grm. sugar, and diacetic acid. Haemoglobin was 68 per cent.;



FIG. 8.—Case 7. Extreme emaciation of "intestinal lipodystrophy."

Roentgenograms of the sella turcica and stomach were negative. There was an old lesion of the upper lobe of the right lung. Hypertrophic arthritis of the dorsal spine was present.

The neurologist noted weakness in power to close the eyelids. The spine was stiff. It was difficult to elicit deep muscle reflexes, but they were finally recorded. Muscle power seemed remarkably well preserved despite emaciation. The absence of subcutaneous fat over the whole body suggested a diagnosis of lipodystrophy.

On dietary restriction and by the aid of insulin (10 units three times a day) the moderately severe diabetes was kept under control, and there was a gain of 6 lb. in weight with general improvement. In February, 1923, pneumonia developed. The patient died six days after onset. Necropsy was not obtained.

Comment.—The patient had always been rather frail, undernourished, and subject to diarrhoea. The loss of subcutaneous fat seemed greater than the loss of muscle. Achlorhydria was noted in one test.

In 1907, Whipple reported an unusual case, that of a man aged 36, who had lost weight and strength during several years. During this time mild diarrhoea was present, the stools containing neutral fat and fatty acids. The patient complained of arthritis and abdominal pain. A few purpuric spots were noted. Acetone appeared in the urine before death. Necropsy revealed large intestinal villi, the lymph spaces of which contained large masses of neutral fat and fatty acid. The tissue between the intestinal glands contained large mononuclear and polynuclear giant cells which had ingested fat. The spleen weighed 375 gm. and the liver 2,570 gm. The pancreas and thyroid gland did not appear to be abnormal. Whipple suggested the term "intestinal lipodystrophy" for the condition.

In 1923, Blumgart reported three fatal cases of a similar nature. The patients were in early middle life, and were markedly emaciated and anæmic, and passed frequent fatty stools. Two specimens tested revealed achlorhydria; in two cases there was acidosis and tetany. Blumgart summarizes the pathologic changes as follows:—

"Pathologically, the significant changes were confined to the intestines and to the mesenteric lymph nodes. In all three necropsies only incidental changes were found elsewhere. The small intestine showed small granular elevations of the mucosa, usually grey in appearance. Microscopically, these elevations were found to consist of phagocytes containing ingested fat. The phagocytes were large and mononuclear, and contained a foamy reticulated cytoplasm. The

mesenteric lymph nodes were noticeably enlarged and hyperplastic, and contained similar phagocytes, with ingested fat."

Tucker, in 1924, reported the case of a youth, aged 18½, who had lost much weight (79 lb.) and much strength over a period of three years. He had obviously lost most of his subcutaneous fat. He passed several loose stools a day. Gastric acidity was normal. The blood-sugar was normal. The basal metabolic rate was -25. The fat content of the stool on an ordinary diet was about 30 per cent.

Case 7 resembles clinically those of Whipple, Blumgart and Tucker, and is presented as an example of "intestinal lipodystrophy." Such cases favour the hypothesis that a disorder of fat metabolism may play a part in progressive lipodystrophy.

DISCUSSION.

The data observed in this series of cases are summarized in the table (p. 165).

The observations in this group tend to support the general opinion that there are a variety of lipodystrophic disturbances which cannot be classified under one heading. It has long been known that the disease is not confined to either sex. It may not necessarily be progressive, and it does not always follow the course of taking fat from the upper part of the body and adding it to the lower part. The chief ætiologic factors in progressive lipodystrophy are as follows:—

Trophic nerve disturbances.—Such disturbances have been suggested as the cause by Barraquer, Simons [23], Long and Bickel, Jolowicz, Gerhartz and Feer. Klein believes that the pineal gland is involved in early life, and that nerve fibres from it to a subthalamie fat-regulating centre produce fat disturbances as well as other trophic disturbances, of which he gives the following list in the twenty-three cases he reviews and reports: Three with hypertrichosis; two with abnormal perspiration; one with acrocyanosis; one with cyanosis of one hand; one with "Warmwellen"; one with polyuria; one with oliguria; one with glycosuria; one with trophic disturbances of nails; one with greyish discolouring of skin; one with pachydermia of face; one with dry hair; one with abnormal sebaceous glandular secretion; one with alimentary glycosuria; and one with rhinorrhoea.

Luce's and Izawa's investigations tend to corroborate Klein's theory. Weber believes that there is a redistribution of fat similar to the redistribution of pigment in vitiligo, as a result of some disturbance in the vegetative nervous system.

Bossert-Rollett reports the case of a girl, aged 4, in whom tic douloureux and nystagmus developed after a fright. Simons [23] and Christiansen have considered muscular dystrophy as a closely allied disease. Christiansen and others have noticed a tendency to nervous and mental phenomena in patients with lipodystrophy. Watson and Ritchie give the impression, however, that these might be merely coincidental. It would seem that the occurrence of nervous phenomena is too common to be mere chance. The possibility that a profound disturbance of fat metabolism might affect the nervous system so rich in fats should be given more consideration. In the case reported by Wolff and Ehrenclou, severe aching pain, soreness and tenderness, especially in the lower extremities, but also in the upper half of the body, were noted. Zondek reported that Sarbo found at necropsy a lesion of the corpus striatum in a case of progressive lipodystrophy. Whether this was coincidental is questionable.

Cases manifesting segmental disturbance suggest basal ganglion involvement. Many phenomena in progressive lipodystrophy suggest disturbance of the nervous system, but they are not conclusive. It is well known that such patients become nervous about their appearance. Whether or not the physiological integrity of the nervous system is impaired is an open question.

Endocrine disturbances.—Another possible cause of progressive lipodystrophy is disturbance of the endocrine system. Klein's hypothesis of pineal disturbances, although applying more especially to trophic nerve disturbance, also applies to the endocrine theory. One of his patients with polyuria, enuresis, and rhinorrhœa, responded to treatment by pituitary. Many writers have expressed the vague belief that the disorder is a combination of endocrine and neurotrophic disturbances. That such a combination may occur is shown by Beck's case, in which obesity of hypophysial origin developed on one side of the body. In further support of this theory are the cases reported by Walsh, in which obesity developed after epidemic encephalitis. Marañon and Soler assert that what occurs in women with this disease is merely an accentuation of their secondary sex characteristics. Case 6 favours this theory. Zondek noted a tendency of patients with hyperthyroidism to retain the subcutaneous fat in the lower extremities. Simons [23] believes that thyroid disturbances are not infrequently associated with progressive lipodystrophy. Marañon and Soler report a series of seven cases showing disturbances of the thyroid gland. One of the cases in my series (Case 1) began during the first of recurring attacks of exophthalmic goitre, while

in two other cases (Cases 2 and 7) basal metabolic rates were high. In one of the cases, however (Case 6), the metabolic rate was low.

That the pituitary gland has some relation to fat metabolism is shown in certain cases of adiposo-dystrophia genitalis and pituitary tumours. Normal and abnormal sellae turcica have been reported in progressive lipodystrophy. Zalla reports a cyst of the pituitary in a case of progressive lipodystrophy that came to necropsy. Sprunt mentions two other cases that came to necropsy in which there was complete atrophy of the thymus in one, and persistence of thymus in the other.

Although the disease usually begins in early life, it has been known to progress in women during the child-bearing period, as in two of my cases. If diabetes mellitus can be regarded as a pancreatic disease, three or four of the cases in the series gave evidence of alteration of function of that organ. Barborka has shown that insulin injected into subcutaneous fat rarely produces local fat atrophy. However, numerous studies of sugar tolerance and blood-sugar in progressive lipodystrophy have been entirely negative. Watson and Ritchie believe that pancreatic function is essentially normal.

Disturbances of fat metabolism.—Such disturbances *per se* may be considered a cause of lipodystrophy. Mirallié and Fortineau, and Hartenberg, by overfeeding, were unable to deposit fat in the atrophic area. Sprunt apparently was more successful, although he administered pituitary in addition to the high calorie diet. Feer found that lipæmia did not ensue after a high fat diet. Simons [23] did not note an increase of blood lipase. Campbell reported excretion of fat through sebaceous glands, but, except for Klein, steatorrhœa has not been reported elsewhere in the literature. From the cases reported by Whipple, Blumgart, and Tucker, one must conclude that there is some alteration in fat metabolism in the group of "intestinal lipodystrophies." Whether this is mechanical or chemical, or both, is not definitely known.

Infection.—The part which infection plays in progressive lipodystrophy is uncertain. Relative lymphocytosis occurs in some cases. Certainly Case 2 of the series seemed infective, and in Cases 3 and 4 the onset followed infections. Certain observers maintain that infections so alter the brain as to permit a nerve trophic disturbance. •

Heredity and race.—There are writers who believe that heredity plays a part. Early writers thought the disease occurred chiefly in Jews. None of the patients in my series were Jewish. The father of one of them died from diabetes mellitus. The uncle of another probably had

diabetes insipidus. The child of one patient had cataracts at the age of 2, and subsequently convulsive seizures and mental deficiency. It would seem that the evidence for hereditary or racial ætiology is inadequate.

Congenital defect.—Frank believes that in progressive lipodystrophy there is a developmental anomaly of the mesenchyme similar to that of osteogenesis imperfecta. He reports a case showing both phenomena. Gezell recently reported a case of hemihypertrophy in a child, and regarded it as a minimal form of twinning. Whether this could in any way explain progressive lipodystrophy remains for future observation and research to reveal.

Pathology.—Except for "intestinal lipodystrophy," which is rare, little opportunity is given to study the pathology of the disease, because it is rarely fatal. However, necropsy data are recorded in four cases of progressive lipodystrophy that showed, respectively, a lesion in the corpus striatum, cyst of the pituitary gland, persistent thymus, and complete atrophy of the thymus. Smith, who examined the skin of a patient suffering from progressive lipodystrophy, summarized its pathological features as follows:—

"The skin is normal in histological structure, except that there is almost complete absence of fat in the tissue beneath the corium. Fat persists in the sebaceous glands, where part of it is doubly refractive. There are very numerous mast cells in the corium, and even in the lower layers of the tissue (McCallum)."

Whipple and Blumgart have described the pathological changes of so-called intestinal lipodystrophy. They found fat-ingesting phagocytes in the intestinal mucosa. Gilchrist and Ketron found similar phagocytes in the skin in their case, which was studied in the acute stages of the disease. It is not known whether such fat-ingesting mononuclear phagocytes are present in all cases in the early stages.

Treatment.—To alter the facial appearance subcutaneous injections of paraffin have been used with only temporary effect. Whole pituitary has been beneficial in a few patients who complained of weakness and nervous symptoms. Ovarian extract seemed to help one of the patients of my series. In view of Sprunt's experience, rest in bed on a high caloric diet should be tried. For the intestinal lipodystrophies nothing has been particularly successful. Tucker believed insulin was giving fair clinical results in his case. Five of the six cases of intestinal lipodystrophy previously reported were fatal.

SUMMARY OF CASES.

Case	Age and sex	Age at onset	Enlargement of liver	Enlargement of spleen	Thyroid	Basal metabolic rate before treatment	Urino	Blood					Nervous symptoms	Diagnosis and remarks
								Sugar	Blood-sugar, gm. per cent.	Hæmoglobin, per cent.	Erythrocytes, millions	Leucocytes	Relative lymphocytosis	
1	49 M.	35	..	..	Palpable	+12 to +45	Trace 1 to 6 gm.	0.125	74	4.84	6,400	..	..	Lipodystrophy facialis (facial hemaitrophy) with exophthalmic goitre
2	27 F.	11 (and 24)	+++	+++	Palpable	+40 and +37	+	0.130 0.135	55 60	2.18 4.04	4,500 5,900	+	+	Progressive lipodystrophy; whole body affected in two attacks
3	31 F.	16	..	..	..	+6	..	0.14	67	4.34	9,400	+	..	Progressive lipodystrophy similar to elephantiasis; following pneumonia and childbirth
4	42 F.	14	..	+	Palpable	+10	..	0.10	72	4.36	5,400	..	..	Progressive lipodystrophy after typhoid (?)
5	23 F.	6	..	..	Palpable	..	..	..	81	4.77	12,000 13,000 14,000	..	..	Progressive lipodystrophy
6	26 F.	18	..	+	..	-13	..	..	76	4.47	7,600	..	..	Recurring lipodystrophy with amenorrhœa
7	50 M.	48	..	..	Nodular	+28, +34	+	0.27	68	3.92	5,200	++	..	Intestinal lipodystrophy; extreme emaciation; diarrhœa; diabetes mellitus

SUMMARY.

The clinical histories of seven patients with lipodystrophic disturbances, examined at the Mayo Clinic, are presented. Two of the cases are unusual: A woman lost all subcutaneous fat, beginning in the lower extremities, in two distinct attacks thirteen years apart. Diabetes mellitus, splenomegaly, and hepatomegaly developed after the second attack. In the other case, a man lost all subcutaneous fat insidiously over a period of two years prior to the onset of diabetes mellitus.

Nervous symptoms, varying in degree and nature, seemed common to the group. The symptoms may be due to the patient's self-consciousness over the change in his appearance, or to physiological disturbance of the nervous system so rich in fatty substances.

Five of the seven cases either had or showed some signs tending towards diabetes mellitus.

Chief among the hypothetical causes are neurotrophic and endocrine disturbances, alteration of fat metabolism, race and heredity, infection and congenital defect.

Little is known of the pathology of lipodystrophic disturbances. In cases in which the skin was examined in affected areas, fat was absent in subcutaneous regions. Fat-ingesting phagocytes have been found in the intestinal mucosa and in the skin in a few cases.

Treatment by means of paraffin injections to remedy the facial appearance has not been permanently successful. A few patients have been benefited by rest in bed, ovarian extract, and whole pituitary.

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ANKLE-CLONUS: THE DISTINCTION OF THE ORGANIC AND FUNCTIONAL VARIETIES.

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THE presence of sustained ankle-clonus is usually considered to be an indication of a lesion involving the pyramidal tract. In certain conditions, however, a more or less regular ankle-clonus can be demonstrated in the absence of other evidence of an anatomical affection of the pyramidal motor system. A clinical aid in determining the significance of foot-clonus under such circumstances has been suggested to me by Dr. Gordon Holmes, based on the simple procedure of bending in sharp plantar flexion the great toe of the foot on which the clonus is at the same time being elicited. If the pressure on the sole of the foot is then maintained constant, and yet the ankle-clonus stops after a certain latent period, a definite "organic" lesion is postulated. If it continues unaffected by the flexion of the toe, it is presumably "functional" in type.

HISTORICAL REVIEW OF ANKLE-CLONUS.

The description of the "Charcot Vulpian Phenomenon," in 1862, appears to have "excited systematic attention" (Gowers) to the study of ankle-clonus. It was known in the literature of that period under different names, among the French as "*trépidation épileptoïde du pied*," a term which has in fact persisted in that country up to the present time. The early accounts of this "spinal epilepsy" were concerned with the rate and amplitude of the movements, their relation to other reflexes and the type of patient in whom it existed. Gowers [1] discussed the subject in 1879, giving a good review of the production and characteristics of clonus, with graphic records in patients with different diseases. He found the latent period to be short, and he was able to start clonic movements in the stretched Achilles tendon "by a tap on the front of the leg"; accordingly he drew the conclusion "that the clonic contractions are the result, not of reflex, but of direct stimulation of (irritable) muscle by the sudden tension or vibration." In 1880 Waller [2] studied the mechanism of the "knee

phenomenon" and of "ankle and knee-clonus"; he regarded them all as being produced by a sudden stretch "that excites muscle fibres to contract," influenced but not "subservied by spinal nervous arcs." In the same year James [3] added to the literature further studies founded on graphic records. Contributions along similar lines by Horsley [4], Herringham [5], MacWilliam [6] and others, followed. In Germany, Erb (quoted by Gowers, q.v.) regarded clonus as a true reflex, but Westphal [7] argued in 1876 that the extensor muscles of the foot are excited to contract directly by mechanical tension, not by the excitation of a reflex. In France, Pitres and de Fleury [8] gave a clear description in 1886 of the features of "*trépidation épileptoïde*" and the factors influencing it, with illustrative records. Their work apparently settled the question of the close relationship between ankle-clonus and the tendon-jerks as definite reflex phenomena.

Attention then centred for some time almost exclusively on whether or not a foot-clonus could ever be entirely "functional" in origin. Gowers had already expressed the definite opinion that it "occurs only in cases in which there is the strongest reason to believe that there is an organic change in the cord." However, he did not deny the possibility that it might be found under other conditions. In 1886 he stated "that for one case of error due to clonus being thought to be due to organic disease when it was really due to a so-called functional state, twenty cases of error have arisen in consequence of the clonus of organic disease being disregarded, its significance being underrated." Mills [9] reviewed the subject later on, agreeing entirely with Gowers. On the other hand, Buzzard is quoted by Playfair, in 1886, as saying, "Ankle clonus, quite indistinguishable from that which was characteristic of lateral sclerosis, occurs in many cases of hysterical paraplegia, in which, on recovery, it ceased to be elicited." Playfair [10] took the same stand himself. Ziehen [11], in 1889, ascribed the production of clonus to any one of several possible causes, including hysteria and neurasthenia. In 1902, a brief article by Weir Mitchell [12] appeared, calling attention to differences in the physiological action of the gastrocnemius and soleus muscles, it being only the latter, according to him, which extends the foot by active contraction in true clonus. Babinski [13] has stated repeatedly that true sustained clonus never occurs in hysteria. He described a "*forme fruste*" which is not sustained. In "functional" states he has found only "pseudo-clonus," which is produced by voluntary or semi-voluntary movements of the foot against pressure. He does admit an intermediary

series of "trepidation" running from "physiological" to "pathological" conditions, but maintains firmly that hysteria as such can bring no such alteration of the tendon reflexes. Incidentally, he appeals to the "skill and finesse of observation" of trained clinicians—for whom, of course, he can speak with greatest weight—rather than to instrumental means, for deciding whether a clonus is true or false. And yet graphic methods of recording foot movements have aided others in drawing a distinction between "true" and "pseudo-clonus," as, for example, Claude and Rose [14]. According to them, the true form occurs in organic disease only, and is characterized by being always regular in amplitude and rate, with a frequency of four to six jerks per second, and by coming to a stop gradually. False clonus ("tremblement") appears in "functional" cases; it is unequal in excursion and rhythm, the jerks may be as rapid as eight to fourteen times per second, and it often ends suddenly. However, in the same paper, they described a hysterical patient who was educated by them to produce a clonus clinically indistinguishable from the true type, and capable of being recognized as functional only by careful scrutiny of graphic records for small irregularities in the movements. Eshner [15] accepted true and false types of clonus, obtaining relatively little effect with either form in the attempt to reinforce the phenomenon as is done with the knee-jerk. Levi [16] contributed observations along the same general lines. He added records of true clonus in persons without disease of the pyramidal tracts, but under deep anæsthesia with chloroform or ether. This effect of anæsthetics had been observed long before then by Money [17], Buxton [18], and others. True clonus in patients with functional disease has been reported by a number of clinicians, including Bechterew [19], Oppenheim, Heard and Diller [20], Brissaud, Déjerine, and Raymond [21]. Potts [22] described a man, considered to have been an absolutely normal person, who presented typical foot-clonus. However, it might be to the point to note that the conception of certain insidious organic diseases was not as well appreciated by those earlier observers as it is now. Disseminated sclerosis, for example, might well have appeared to be a purely functional disorder in its initial stages, especially if the signs cleared up in a remission. In fact, Ballet [23], [24], published the findings in an instructive case in an even better recognized group; a 46-year old man was diagnosed in 1903 as neurasthenic with a transient foot-clonus, but he returned in 1905 with a definite syphilitic meningitis.

Several articles have appeared with authentic records of ankle-clonus

occurring in patients with infectious diseases or with other toxic states. Strümpell [25] found it in certain cases of typhoid, tuberculosis, and in other conditions where there was emaciation unassociated with other evidence of disease of the central nervous system. Curschmann [26] described clonus in uræmia, and suggested that the appearance of clonus in a patient with severe kidney disease can be a warning of an impending uræmic seizure. Tileston [27] reviewed the literature up to 1913, added some cases of his own, and gave in his summary a list of causes of foot-clonus not due to disease of the pyramidal tracts, namely, acute infectious diseases, chronic infections with toxæmia (especially tuberculosis), uræmia shortly before and during the acute uræmic seizure, epilepsy immediately after the convulsion, intoxication from certain drugs (e.g., hyoscin, ether, chloroform), excessive fatigue, exceptional cases of certain neuroses, psychoses in a stage of excitement, and chronic articular rheumatism.

The more recent literature still shows difference of opinion. For example, Noica [28] and Radovici [29] believe true clonus always to be a sign of pyramidal lesion. Lemos [30] agrees with that view, basing his argument in part on the response of post-encephalitic Parkinsonism with clonus to scopolamine. Although scopolamine produces a prompt cessation of such a clonus, there is an exaggeration of clonic foot movements after the immediate effect of the injection has worn off. On the other hand, Guillain and Barré (quoted by Pereira, q.v.), in 1916, denied sharp distinctions between true and false clonus. They obtained electric changes in the muscles of healthy persons, which were sufficiently like those occurring with interruption of the pyramidal tracts to make them consider clonus possible under normal as well as in pathological conditions. Sollier [31], in 1921, distinguished cases which had an active contraction only of muscles of the calf ("simple" clonus) from those which showed an alternating active contraction of the flexors and extensors of the foot ("alternating" or "pseudo-clonus"). Either type might occur with hysterical or with organic contractures. Souques [32] reported true clonus with peripheral nerve lesions, secondary in some cases to arthritis. Westphal [33] recorded two patients with dementia præcox who presented ankle clonus, there was no spasticity of the extremities, but some muscular atrophy.

The most exact clinical contributions have been made with the help of the string galvanometer. In 1910, J. K. A. Wertheim Salomonson [34] described ankle-clonus as consisting of a series of separate muscular contractions, taking cases of lateral sclerosis as a paradigm. Each extensor

twitch of the foot was preceded by a single diphasic action current in the foot-extensor muscles. In the intervals the string was practically still. In hysteria, on the other hand, the electromyogram showed marked oscillations of irregular amplitude with regular larger waves, one immediately before each clonic muscular contraction which was indicated by a mechanical myogram. In addition there were smaller waves interspersed throughout the record, suggesting a "voluntary tetanus." Where there is organic clonus, he postulated, there is a true hypertonus of the muscles, while in functional disease voluntary impulses are necessary to raise the muscle tone enough to allow the production of a foot-clonus. In 1920, Salomonson reviewed the subject and stated that electromyograms provided "the only absolute and reliable symptomatic and genetic difference between the two conditions." Gregor and Schilder [35] made extensive studies of the action currents in a number of pathological conditions. Their results tended to break down the sharp distinctions made by Salomonson between organic and hysterical clonus. Whereas they also obtained in some records single diphasic action currents with each clonic thrust of the foot and clear intervals between them (e.g., fig. 40, p. 412), they found various combinations of this simple rhythm and of superimposed waves in the hand- and in the foot-clonus of spastic extremities. The usual picture of true clonus showed one or two, less often three, action currents for each movement of the foot. Secondary deflections of the string did not seem to be due to "interference" at the "equator" of the muscle. But they were able to demonstrate a continuous gradation in the electromyographic picture between a purely voluntary imitation of clonus in a healthy person (c.f. "hysterical" clonus), the voluntary movements in a spastic limb in hemiplegia, and a totally involuntary clonus as ordinarily elicited in a patient with spastic hemiplegia. Cobb [36] added electromyographic studies in 1918. He included in his report two cases which showed a tetanic series of waves resembling those described by Salomonson as "hysterical." One of them was obviously organic; the other had a post-typhoidal clonus without an extensor response of the great toe, and this patient "liked to balance his foot so it would jerk." The most interesting point in Cobb's article is his insistence on viewing clonus as merely a phase of reflex activity lying between that of normal tendon-jerks and that of spasm. Consequently, he discards pigeon-holes in his classification of clonus for clinical diagnosis. Pereira [37] reviewed the literature to 1925, with emphasis on the French contributions. From the observations of

others, and from his own electromyograms, he concluded that there are not two kinds of clonus, that due to pyramidal disease and functional; either clonus exists and is then merely a reflex, increasing continuously from physiological to pathological importance, or else clonus does not exist, and in that case one meets with definite voluntary contractions of the foot. There is a prolonged shortening of the extensors of the foot, which may be voluntary (physiological) or involuntary (pathological). Superimposed on that there are then simple contractions, which make up the clonus. In the electromyogram, each initial large wave preceding a clonic jerk of the foot is thought to originate in the soleus muscle; the smaller additional waves are believed to represent overflow to other muscles in the extensor group.

THE FLEXION REFLEX.

According to Babinski [38], Prochaska, in 1784, was the first to study flexor withdrawal of the leg and foot on unpleasant stimulation of the lower extremity, in patients with injury of the spinal cord. Charcot has been accredited with exciting the same type of response in similar patients by brusque plantar flexion of the great toe. Many others have since reproduced those manœuvres. No attempt will be made here to review the literature on this reflex. It has been well done by Walshe [39], under the heading of "flexion reflex," by Riddoch [40], who called it the "mass reflex," by Babinski (q.v.) as one of the "reflexes de défense," by Öwre [41], under the title of "reflexes of spinal automatism," by Filimonoff [42], as an "Abwehr-reflex," by Minkowski [43], in a developmental setting, phylogenetically and ontogenetically, and by others.

The flexion reflex implies, as a rule, a definite organic lesion in the spinal cord, but it is also known to occur physiologically in normal persons in a somewhat altered form. According to Babinski, a clear distinction can be drawn between the physiological and the pathological type of response. Under purely physiological conditions there are greater rapidity of withdrawal, shorter duration, more prompt return to the original position, a more uniform amplitude of movement, and finally—and most important—there is flexion merely at the hip and knee but not of the foot at the ankle. "Triple flexion," at the hip, knee and ankle, is always, according to him, a sign of organic disease.

ANTAGONISM BETWEEN ANKLE-CLONUS AND THE FLEXION REFLEX.

As early as 1866, Brown-Séquard [44] published in a footnote to an article certain observations made with other physicians on the

relation of the flexion reflex to foot-clonus. From that statement it seems to have been common information by that time that a sustained clonus could be brought to a stop by sharp plantar flexion of the great toe. He said: "The influence of an external irritation in producing a favourable change in the nervous centres is beautifully illustrated in cases of myelitis existing in a small zone, in the upper or middle part of the dorsal region, leaving below it all or nearly all the dorso-lumbar enlargement of the spinal cord almost in a healthy condition. In four well-characterized cases of that kind that I have seen, one of them with Professors Trousseau and Nelaton, another in consultation with Dr. Verneuil, and a third, an hospital patient seen by my colleagues, Dr. Ramskill and Dr. Hughlings-Jackson, there were, as usual in such cases, extremely violent and frequent reflex spasms in the lower limbs. In every instance these spasms at once abated and quickly ceased when the big toe of either of the feet was seized and forcibly drawn down, flexed as much as the ligaments of the joints would allow." Westphal [7] mentioned using the same procedure in Germany in 1876. Clinical studies continued to be made on the flexion reflex and on ankle-clonus. But the relationship between them was apparently dropped until 1912, when Marie and Foix [45] revived it with the addition of further physiological explanations on a basis of reflex inhibition. In the meantime, the experiments of Sherrington [46] gave exact definition to "nociceptive" (painful) stimuli, as well as to "proprioceptive" stimuli (due to "movements active and passive of the limb itself, producing changes in shape and tension of muscles"). Whereas the superficial methods of eliciting the flexion reflex in man (scratching, pinching, pricking the skin, or applying hot or cold water, &c.), are all purely nociceptive—the deep stimuli (squeezing the foot, or flexing the great toe) are at least partly proprioceptive. The procedure of checking foot-clonus by toe-flexion, then, may be considered due in part perhaps to a defence mechanism (nociceptive in origin), but mainly to the response to stretch in the anterior musculature of the leg (proprioceptive), apart from any protective withdrawal. Walshe discussed clinical features of "reciprocal innervation" in the flexion reflex, stating that the spastic extensor tone which allows the production of clonus is inhibited on that basis by eliciting a phasic flexor reflex. He refers to the long-recognized fact, as an example, that "clonus of a spastic limb could be stopped immediately, and the limb rendered 'perfectly supple and pliable' by forcible plantar flexion of the hallux."

Further, practical application of this principle appears in the nursing

lore of certain institutions, in which toe-flexion is commonly used as an efficient way of breaking an extensor rigidity too resistant to yield in nurses' hands to ordinary manipulation. Riddoch has mentioned stopping ankle-clonus with toe-flexion, giving in the same article many other examples of reciprocal relaxation of postural reflexes by the production of antagonistic reflex reactions. In 1923 Froment [47] reported similar inhibition of foot-clonus. He had graphic records to show the relationship. They proved that an arrest of the clonus occurred, but also suggested that it was not on a basis of strictly antagonistic reciprocal innervation. He found that heterolateral crossed extension would give the same cessation of clonus as is obtained by the homolateral flexion reflex. Hence, he believed checking clonus by either means to be an "active phenomenon" in which the foot is caught and fixed in flexion by a synergic contraction of antagonists. The synergic action which stops clonus when a heterolateral crossed extension reflex is elicited, includes definite contraction of the gastrocnemius muscle, as well as of the soleus. It is the latter muscle alone which is considered responsible for maintaining "true" clonic movements of the foot. Pereira mentioned in his review of ankle-clonus its relationship to toe-flexion without adding anything new about this particular feature. Rouquier and Couretas [48] made a differential study of clonus as it exists with lesions of the pyramidal tract, in comparison to the false clonus of functional disorders, and finally to clonic foot movements occasionally seen in post-encephalitic Parkinsonism. Pyramidal clonus consists of equal and regular contractions, caused only by the soleus muscle without intervention of the gastrocnemius, persisting when the subject is placed in ventral position; there is no voluntary movement and the clonus is inhibited by "reflexes de défense." False clonus is provoked by "global contraction" of the gastrocnemius and the soleus, disappears in ventral position, has oscillations of greater frequency and of more irregular form and rhythm; it can be produced voluntarily in some subjects, and occasionally it may occur as secondarily to peripheral irritation, in which case it may take on the characteristics of pyramidal clonus. Parkinsonian clonus is quite as regular as the pyramidal form, has large amplitude, is involuntary, persists in the ventral position, does not depend on contraction of the gastrocnemius, is associated with an exaggeration of reflexes of posture, is not inhibited by "reflexes de défense," but disappears under scopolamine ($\frac{1}{2}$ mg. subcutaneously).

Neat demonstrations of the mechanism involved in arresting clonus by toe-flexion are furnished in the physiological laboratories. In 1924

Liddell and Sherrington [49] showed that stretch applied to a muscle provokes contraction in it. They choose the knee-extensor for their experiments on decerebrate preparations. The stretch itself provides a proprioceptive stimulation of receptors lying in the muscle. These investigators produced evidence suggesting that the knee-jerk and patellar-clonus are fractional examples of the more comprehensive stretch reflex. They were then able to inhibit those reflexes by stimulation of certain afferent nerves: the peroneal, popliteal, or saphenous nerves on the same side. Plantar flexion of the hallux would excite proprioceptive impulses in the nerve to the extensor longus hallucis muscle—which is a branch of the N. peroneus profundus (anterior tibial)—one of the nerves used by Liddell and Sherrington to abolish contraction in the knee-extensor muscle in their preparations. Furthermore, Viets [50] had previously shown that he could raise the extensor tone of leg muscles in a spinal animal by contralateral peripheral nerve stimulation, so that a clonus would result as soon as the tonic tension of those muscles became high enough for a series of continued self-sustaining twitches to take place. Stimulation of the corresponding homolateral peripheral nerve decreased the tonic tension and suppressed patellar-clonus, just as was found to be the case by Sherrington.

PROCEDURE.

The arrest of ankle-clonus by plantar flexion of the homolateral hallux has been put into effect during the examination of a number of patients in The National Hospital, London, and elsewhere, by Gordon Holmes and the writer. The technique is so simple that it needs no special description. It merely consists of eliciting foot-clonus in the ordinary way. Then, while it is being maintained with constant pressure on the sole of the patient's foot, the great toe is bent forcibly in plantar flexion. The results have usually turned out as expected from other findings or from the further development of the case. Only on a very few occasions did sustained flexion of the toe fail to inhibit the clonus in cases which were obviously organic from other signs. Quite a difference in the latent period was noted in different individuals. There have been no instances among these observations in which hysterical clonus failed to continue in spite of prolonged forceful toe-flexion. However, few examples of functional foot-clonus were investigated, and theoretically there is reason to believe that there may be considerable variation in the response of hysterical patients as well.

In order to obtain graphic records, an apparatus was devised (fig. 1) which has incidentally reduced certain possible objections to the technique of the clinical procedure. It operates on the principle that the force exerted in flexing the great toe acts on the fixed point, O, at the axis of the ankle-joint, and that the arm, OA, prevents any shortening other than that along the vector, AB, since the lever, CB, is the only moving part in the system through which the forces act. A string passes from the fulcrum, O, over pulleys to the end of the lever, CB. Tension on the string draws the great toe downward in plantar flexion toward the arm,

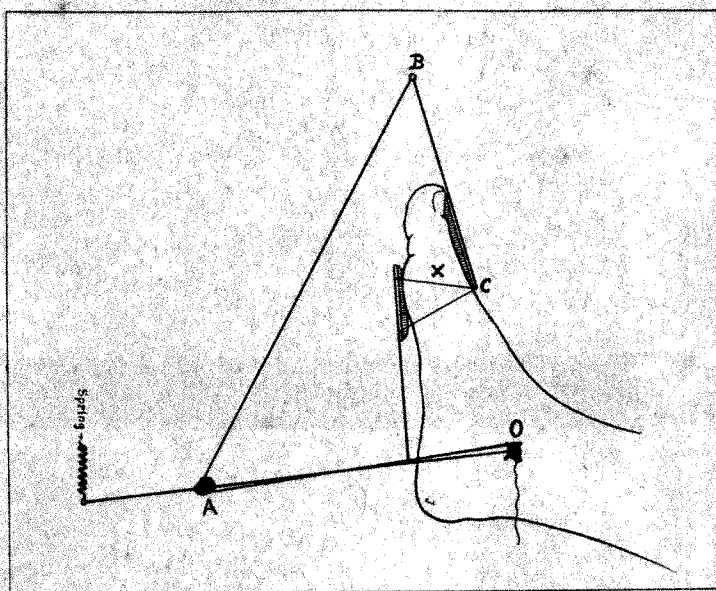


FIG. 1.

OA. That arm remains in a fixed position in relation to the rest of the foot, moving with it in clonus and without changing in any way the pressure of the rigid framework against the sole of the foot. The clonus is maintained, quite independent of the lever action on the toe, with a pressure which is regulated by using springs of different sizes. Their tension can be altered as needed before each record by moving a small clamp up or down on a vertical rod. The leg is loosely suspended at the knee and ankle, and the foot is clamped as tightly against a thinly-padded support along the ball of the foot as comfort will allow. Accordingly, actual shortening of the extensor muscles on the sole of the foot when the great toe is flexed is considered practically impossible.

Finally, the patients on whom records were obtained stated (with one exception) that they felt no appreciable discomfort throughout the procedure. The exception had a hysterical type of clonus, which neither muscle-stretch nor pain at the time of the toe-flexion could stop.

Two records have been selected by way of illustration.

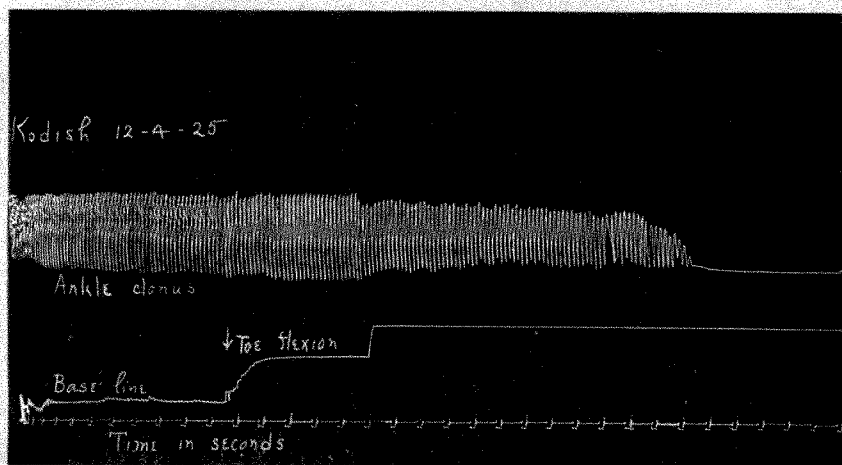


FIG. 2.

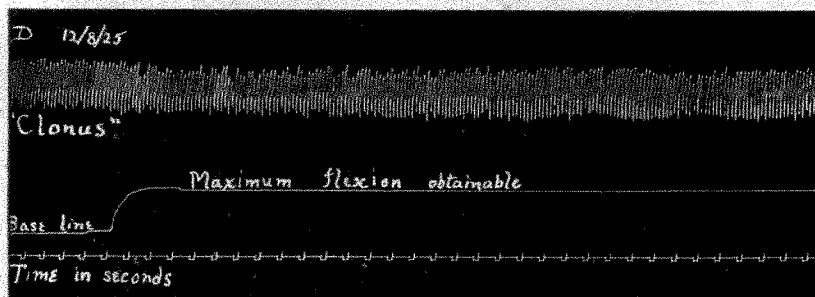


FIG. 3.

Fig. 2 (Kodish). Syphilitic meningo-myelitis with organic clonus, arrested by forceful plantar flexion of the great toe.

Fig. 3 (B.S.). Functional disorder with compulsive blepharospasm and "hysterical" clonus, which could not be checked by toe-flexion.

DISCUSSION.

The actual procedure of superimposing the response to sharp plantar flexion of the hallux on ankle-clonus is extremely simple, and it

can be quickly done during a routine neurological examination without loss of time. The fact that it has been used with limited application for over sixty years speaks in favour of the technical facility with which it can be carried out. The rationale has received perfectly sound support from the physiological laboratories, where clonus of extensor muscles of a leg has been repeatedly abolished by stimulation of homolateral nerves, containing afferent fibres, lying in the region of distribution to flexor muscles. Stretching a muscle—as is done in toe-flexion—gives adequate proprioceptive stimulation to arrest a clonus of the antagonistic muscles. If carried out quietly, no patient could be expected to realize the significance of the manoeuvre. Cessation of a clonus could hardly be attributed to suggestion from mere manipulation in the test, but, on the other hand, the observer is left free to utilize whatever verbal suggestion he may care to introduce. In the results reported here, no attempt was made to influence the patients; they were treated alike in action and in talk.

Occasionally flexion of the hallux failed to stop an ankle-clonus in the case of patients with organic disease probably involving the pyramidal tracts. The explanation for that was not always clear. But the briefest consideration will provide structural and mechanical reasons for difficulty in stretching the extensor hallucis longus muscle appreciably by merely flexing the great toe on the foot in some persons. That is particularly so if there is any tendency toward arthritis. Sherrington has shown that the bulk of proprioceptive fibres responding to stretch lie in the belly of a muscle rather than in the tendinous attachment. Consequently change of position of the hallux at the joint surface would not in itself give the same intensity of stimulation as would tension on the extensor muscle of the great toe. Furthermore, the results from joint sense alone would not be selectively directed along nerves which innervate the flexors. The same applies, of course, to the procedure of squeezing the foot, which has at times been used instead of toe-flexion in eliciting the flexion reflex.

There is also a possibility of introducing into the act of brusque toe-flexion enough discomfort to the patient to provide a distinct nociceptive as well as proprioceptive factor. But, in organic cases, the literature as well as our own results lead one to expect clonus to stop anyway, whether proprioceptive stimulation exists alone or is augmented by a nociceptive element. In functional cases the addition of pain is best avoided, but even if it does occur it does not necessarily invalidate the result. Failure to check clonus in spite of pain occurred at least once

in this series of observations, and that fact increases the likelihood of the clonus being on a strictly functional basis. Moreover, the physiological withdrawal from nocuous stimulation of the foot is specifically stated by Babinski to take place only at the hip and knee; according to him, then, even that move would not include dorsi-flexion of the foot at the ankle. The balance would not be broken at the ankle-joint where the clonus is going on.

It has been suggested by colleagues that flexion of the great toe might shorten slightly but perceptibly muscles on the sole of the foot, which are components of the extensor mechanism. That might be the mechanism which brings clonus to a stop. This suggestion is valid in so far as it adds another physiological factor which may play a part, but it seems hardly possible that it could affect the records obtained on the apparatus described in this paper, since the ball of the foot was very firmly clamped to a support, allowing no observed motion of the foot itself. Toe-flexion repeatedly arrested organic clonus under those conditions, and so it seems likely that the clinical procedure has much the same balance of elements—predominantly an antagonism of reflexes, possibly an additional slight shortening of the extensors of the foot. This does not, however, affect the significance of the test in regard to organic and functional clonus.

Obviously the observer, although intent upon toe-flexion, must guard against unwittingly relaxing pressure against the sole of the foot while the clonus is being maintained.

It may be of interest to bring up more theoretical considerations. Tendon-jerks are subject to considerable variability under different conditions. They may be absent or minimal on waking up in the morning, are distinctly exaggerated after exercise or too much coffee, and are more so after certain other drugs, such as adrenalin [51]. Emotional factors have a marked effect. Suggestion, "will," hypnosis [52], [53], are reported to be capable of altering tendon reflexes. As one of the successive stages of reflex activity, ankle-clonus appears when there is a sufficient increase of tone of the extensor muscles of the foot [54]. This is not considered identical with the observation of Gowers (q.v.), Weir Mitchell (q.v.), and others, who called attention to the possibility of obtaining an involuntary clonus by the soleus muscle in normal persons without their having distinctly increased extensor tonus of the legs. "Let any healthy man sit forward on the edge of a chair with the leg in at least 45° of flexion; let the weight of the leg rest on the toes. If needed to aid the production of clonus, press down with the hand on the knee. It is easy

then to start the movement. It may go on for minutes, an entirely unwilld action."

Physiological limits of reflex activity are known to merge indefinitely into the pathological along various lines. Even the plantar response described by Babinski as pathognomonic of pyramidal lesion has been repeatedly found in certain "toxic" states where no anatomic destruction of the pyramidal tract has been demonstrated (Elliott and Walshe, [55], *et al*). It seems that true foot-clonus may occur under certain conditions, as anæsthesia (Money, Buxton, Levi, q.v.), infections and other toxic states such as uræmia (reviewed by Tileston, q.v.), etc. To intimate that pathological physiology rather than pathological anatomy may bring out a true foot-clonus shows no disrespect for its relation to pyramidal function.

If then such sharp distinctions in ætiology of clonus are unwarranted, one could not expect the simple procedure of plantar flexion of the hallux to settle definitely the differentiation between organic and functional origin in all cases. Moreover, it might be hard to classify as physiological or pathological the flexor withdrawal of the leg in response to toe-flexion under the conditions in which it is elicited together with clonus. Hence their combination should not be considered infallible. The importance of the whole test, it seems, lies in the opportunity it gives to catch a patient in a pitfall; those "hysterical" subjects who are nearest akin to malingerers should fall the hardest; those whose clonus springs from a physiologico-toxic cause are less likely to be caught; patients with definite pyramidal lesions are expected to escape entirely, reacting properly according to the law of antagonistic reflexes.

SUMMARY.

(1) Although usually associated with a pyramidal lesion, sustained ankle-clonus may occasionally have a physiological or "functional" ætiology.

(2) A rapid and simple test is offered as a clinical aid in distinguishing "organic" from "functional" types of clonus.

(3) It consists of forcible plantar flexion of the homolateral hallux while ankle-clonus is being maintained. If the clonus is then checked, an organic lesion in the central nervous system is postulated. If it persists in spite of prolonged toe-flexion, it is probably "functional" in origin.

(4) The mechanism of cessation of ankle-clonus by flexion of the

great toe in organic disease depends on an antagonism of reflexes. Clonus requires increased tone of the extensor muscles of the foot. Forceful plantar flexion of the hallux gives rise to the withdrawal or flexion reflex in which there is strong tonic contraction of the dorsiflexors of the foot. That flexor contraction causes reciprocal relaxation of the opposing extensor muscles with consequent disappearance of the clonus. Plantar flexion of the great toe provides stimuli which are largely proprioceptive and which make up the sensory portion of the arc relating to the flexion reflex.

(5) This procedure has been described before, although the application has usually not been made in differentiating these two forms of clonus.

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TRAUMATIC ANEURYSM OF THE INTRACRANIAL PORTION OF THE INTERNAL CAROTID ARTERY.

BY J. L. BIRLEY, M.D.

WITH A NOTE

BY WILFRED TROTTER, M.S.

WITH one exception, injury to the intracranial portion of the internal carotid is summarily dismissed in the textbooks of surgery as being almost invariably fatal. The exception is the traumatic arterio-venous aneurysm in which a communication develops between the artery and the adjacent cavernous sinus. An arterio-venous aneurysm of this nature, usually a complication of fracture of the base of the skull, is the immediate cause of a majority of the cases of "pulsating exophthalmos." In this condition, in addition to the pulsation and protrusion of the eyeball, the conjunctival and retinal vessels are distended, the movements of the eye restricted and, finally, the whole globe tends to become disorganized as a result of increasing dislocation and vascular engorgement. The condition is further characterized by a loud and continuous bruit, audible on auscultation over the orbit and distressingly audible to the patient. A search through the archives of medicine, surgery, and ophthalmology has failed to reveal any example of injury to the intracranial carotid, apart from those which are immediately fatal or those which are productive of pulsating exophthalmos. This communication deals with such an exception, and is presented for the reasons that there appear to be no good grounds for assuming that a similar state of affairs might not be encountered in the future, that the condition can be accurately diagnosed and, as in the case herein described, is amenable to surgical intervention.

SUMMARY.—*Male, aged 23. On April 27, 1924, he was involved in a motor accident in Canada, sustaining serious head injuries which rendered him unconscious. On admission to hospital his pulse was 80, blood-pressure 100/50 mm. Hg. and his right pupil dilated and fixed; complete flaccid left hemiplegia. Consciousness began to return a few hours later, and within forty-eight hours there had been a very considerable recovery of power in the left arm and leg;*

there was paralysis of the left sixth and seventh, and the right third, fourth and sixth cranial nerves, with diminution of vision in his right eye. Rapid improvement in general condition followed. On June 9 and 10, epistaxis.

After arrival in England on August 1, 1924, he was convalescent, but suffered with recurrence of epistaxis at varying intervals and of varying amounts. State on September 4: Memory defective, slowed cerebration; pallor of right optic disc with diminished visual acuity and visual fields; paresis of the right third and fourth and of the left sixth and seventh; no hemiplegia; no proptosis, or bruit over skull; nasal examination negative. September 20: Blood-count: red cells 5,500,000 haemoglobin 79 per cent, colour index 0.7, marked basophilic changes in red cells. Between September 30 and October 7, three attacks of profuse epistaxis, two of which nearly proved fatal. October 7: Ligature of the right internal and external carotid vessels just above the bifurcation, followed by rapid improvement, and culminating in complete restoration of mental and bodily health, together with disappearance of all physical signs, save for a right mid-plegia and slight impairment of vision in the right eye.

DETAILED CLINICAL DESCRIPTION.

A. G. C., male, aged 23. On April 27, 1924, after a "hectic" night, at 6 a.m. a closed motor car, in the back seat of which he was sitting, left the road and hit a telegraph pole. The body of the car came off and he was picked up some distance away on the roadside unconscious and bleeding from a wound on the right side of the head. Of the two other occupants of the back seat, one sustained a fractured arm and cuts about the face, while the other was unhurt. The driver had his nose broken and the other occupant of the front seat was uninjured. The patient was brought a distance of some twenty miles, and admitted to the Toronto General Hospital at 8.15 a.m.

On admission he was unconscious, pulse 80, respirations 24, sighing, blood-pressure 100/50. There was bleeding from the left ear. The right pupil was dilated and fixed and inactive to light. There was ecchymosis of both lids of the left eye; the left pupil was small and reacted to light. It was noticed that whereas he moved his right limbs, the left arm and leg lay limp and flaccid. Plantar reflexes were absent, the knee-jerks were active and equal, but no tendon reflexes were obtainable in the left arm. There was a scalp wound, about $3\frac{1}{2}$ in. long, running sagittally $\frac{1}{2}$ in. to the right of the middle line on the anterior part of the top of the head. No depression of the skull was seen or felt. 9 a.m.: The periosteum was stripped off the bone for 1 in. on either side of the scalp wound. A fissured fracture crossed the posterior part of the scalp wound almost at a right angle. No attempt was made to follow this fracture beyond the part exposed by the wound. The scalp wound was closed by silk-worm gut after cleansing, and several smaller cuts were also closed. During the operation of suturing the patient objected and raised the right hand repeatedly, and attempted to express himself in words without success.

At 9.40 a.m., pulse 110, blood-pressure 100/50. During the next thirty-six hours the blood-pressure gradually rose, reaching a systolic pressure of 150, after which it gradually fell again to 120. Within about four hours of admission the patient could be roused, but if left alone he remained perfectly quiet and asleep. For the first forty-eight hours it was necessary to empty the bladder by catheter and the bowel by enema. It was noticed on the second day that the right knee-jerk was brisker than the left.

April 30.—Condition had now improved and he complained of pain in the neck and right shoulder. There was some rigidity of the neck muscles when an attempt was made to bring the head forward. The fundus oculi was normal on each side. A small laceration of the mucous membrane over the hard palate was discovered, about 1 in. long and to the right of the middle line. There was no deformity along the infra-orbital margin. A complete facial paralysis of the left side had now developed which was not observed on admission. There was a marked recovery of power in the left limbs. The patient was unable to move either eyeball past the middle line to the left.

The patient showed a gradual improvement in his condition. As he regained consciousness he developed a moderate degree of cerebral irritation, and towards the end of the first week he tried to get out of bed and became restless. His subsequent progress was entirely satisfactory, and an X-ray examination was carried out on June 2. The plates showed a radiating fracture of the right parietal and temporal bones, with one limb of the fracture radiating downwards and disappearing in the middle fossa, immediately in front of the right petrous bone. A slight, shallow depression was also present.

June 10.—Ptosis of the right eye and loss of inward, outward and downward movement of the right eye and of outward movement of the left eye. Paralysis of the left seventh nerve persists. On this day he was kept waiting for some time in a hot room, and just as he was put into position to be X-rayed he had an hæmorrhage from the nose which could not be controlled for an hour.

June 12.—The patient left the hospital and went home and gained strength from day to day, coming downstairs as soon as dressed in the morning about 11 o'clock.

June 19.—Another epistaxis which lasted two hours.

June 25.—The optic discs show definite pallor, more marked in the right eye, without gross defect of vision or diminution of visual fields. Taste and smell normal. Paralysis of the right third nerve is no longer complete, and eyelid can be raised. Right pupil inactive to light and accommodation. Paralysis of the left sixth nerve still complete, that of the left seventh nerve no longer complete. Other cranial nerves normal. The deep reflexes of the left arm and leg are slightly brisker than on the right side. Plantar responses normal. Left abdominal reflexes diminished as compared with the right. No evidence of any injury to the spinal cord.

June 30.—Examination of the nose and throat revealed no explanation of the hæmorrhage from the nose.

On *July 12* he left Toronto for the country. By this time he was permitted to smoke, take a little alcohol, bathe, walk, row, paddle a canoe, play golf, and read a little. His condition rapidly improved, and on *July 23* he went to Montreal and sailed for England on the 25th. He was very well on the voyage, and on arrival at Liverpool on *August 1* he proceeded to the Lake country. The patient was now going for motor drives, and he began to play golf very gradually; a few holes at first, then 9, then 18. He bathed on one occasion, and had a cold bath every morning.

On *August 11* he played 18 holes of golf and one set of tennis, and woke up the next morning, *August 12*, to find his nose bleeding; the bleeding continued for three hours. On this day he had a slight headache, the first he had had since leaving the hospital.

August 17.—He woke up with a slight headache, and in the afternoon, while out for a short walk, his nose bled again very slightly.

August 19.—While getting out of his cold bath in the morning, the hæmorrhage from his nose came on very violently with a great gush. He was unable to make anyone hear him and, feeling faint, lay down on the floor, and after some distress fainted, still without any clothes on. He was in the bathroom about three-quarters of an hour, and when found he had been able to put his dressing-gown on and to open the door. He remained in bed all that day, feeling weak and with a slight headache. The next few days he felt weak and had a headache and was kept very quiet. Very slight hæmorrhages occurred in the morning on *August 22, 23 and 24*.

September 4.—Examination. In addition to the hæmorrhages from the nose already described, it transpired that ever since the accident, both in the hospital in Canada and since leaving it, the patient had had mucus stained with blood dropping from the back of his nose into his throat, which he usually noticed when he woke up in the morning. Ever since the severe hæmorrhage on *August 19* this had occurred every day until the last three days, during which he had been quite free. There had never been any other discharge from the nostrils.

Mental condition.—He has no recollection of the accident and can remember practically nothing of the incidents of the evening preceding the accident, when he was at a dance. Ordinary memory is now improving, but he is forgetful of details. He finds he is slow in making any calculation, although previously he had no difficulty in doing this, having been trained as a chemical engineer. He can read a simple book for half an hour without getting tired. Noise, company, &c., do not bother him in the least. Sleep excellent, and no dreams.

General condition.—Is distinctly pale and the mucous membranes are slightly blanched. The viscera are all normal and the heart sounds are closed. He is well-developed and of exceptionally good physique, both mentally and physically. Cranial nerves. The right optic disc is definitely paler than the left; visual acuity $\frac{6}{8}$. Colours not so well seen as with the left eye. There is slight concentric contraction of the visual fields of the right eye, more marked

to blue than to white. The right pupil is moderately dilated and inactive to light and accommodation. Upward, downward, and inward movements of the right eye are defective. There is slight vertical diplopia, most pronounced on looking down and to the left, and there is also defective action of the superior oblique in addition to the oculomotor paresis. The left optic disc is normal; visual acuity $\frac{5}{6}$; visual fields full. There is paresis of the left external rectus muscle, and there is slight weakness of all the muscles of the face on the left side. Other cranial nerves are all normal. There is no evidence of a left hemiparesis, beyond the fact that the tendon-jerks on the left side are, if anything, brisker than those on the right. The abdominal reflexes are present and equal on both sides, and both plantar responses flexor. There is no headache, no proptosis, and no bruit is audible over the skull. There is no clinical evidence of any fracture of the cervical spine.

It was obvious that the patient had sustained a fracture of the vault of the skull on the right side, one limb of which had radiated down to the base, across the middle line, to terminate in the neighbourhood of the apex of the petrous bone on the left side. His general appearance did not seem to fit in with any really severe hæmorrhage, and it was thought that possibly the amount of blood lost had been unwittingly exaggerated. At the same time, the true explanation of the source of the hæmorrhage was not arrived at. There were none of the ordinary signs of a carotid aneurysm communicating with the cavernous sinus, and it was supposed that the hæmorrhage might have proceeded from granulation tissue round some necrotic bone at the base of the brain, communicating with the sphenoidal sinus.

Treatment.—His activities were firmly curtailed, both mental and physical, and all exercise forbidden except that of gentle walking.

September 5.—Examination of nose, ears and throat, by T. H. Just. The nose is normal and no bleeding point can be discovered in it. Both antra and frontal sinuses are quite bright to transillumination. With regard to the ears, both drums are intact and rather pale. Hearing in the right ear is normal and there is slight loss of air conduction in the left ear. The bone conduction and the range of high and low tones are normal in each ear.

September 9.—About an hour after his morning walk the hæmorrhage from the nose came on again with a rush, but was controlled in a short time with little loss of blood.

In view of the recurrence of hæmorrhage from the nose, he was admitted to a nursing home on September 12. Further questioning elicited the fact that a slight headache nearly always preceded the more severe attacks of hæmorrhage.

During the next fortnight he was given two injections of hæmoplastin, with a view to increasing the coagulability of the blood. At the end of that time his general condition had improved, but he occasionally found a little blood at the back of his throat, especially on waking. He also complained of a certain amount of persistent right-sided headache, which was a new development. On the other hand, there was some recovery in the function of the left external rectus muscle and of the muscles supplied by the left seventh nerve.

Examination of the blood on September 20, by Professor L. S. Dudgeon, gave the following results. Red cells 5,450,000 per c.mm.; hæmoglobin 79 per cent: colour index 0·7; leucocytes 7,600 per c.mm., polymorphs 58 per cent., small lymphocytes 28·5 per cent.; large lymphocytes 4·0 per cent., large hyaline 5·5 per cent.; eosinophiles 3·5 per cent., neutrophilic myelocytes 0·5 per cent., marked basophilic changes in red cells., no nucleated red cells seen, platelets numerous. The results of the blood examination unfortunately tended to confirm the suspicion that the amount of blood lost had been exaggerated.

September 27.—Physical signs unchanged, but right visual acuity now $\frac{6}{24}$.

On the evening of September 29 he had some right-sided headache and felt feverish. His temperature was 100·6° F., pulse 92, and the throat was slightly injected and there was a hard, dry cough. He appeared to have a mild attack of influenza and was kept in bed. On the evening of the 30th he had a moderately severe hæmorrhage from the nose while in the bathroom. The bleeding seemed to come from the right nostril before the left. It lasted about twenty minutes. When seen in the early morning of October 1, he was not blanched, had no headache, and seemed fairly well. His temperature was normal, his cough looser and the throat clear. The following day he felt quite well and sat up in a chair in the evening. He went to bed and slept normally until 4 o'clock a.m. on the 3rd, when he woke up to find that he was bleeding from both nostrils. He was seen about 4.30 a.m., and found to be prostrated, blanched, and drenched with blood, with a running pulse of about 140. At that time the bleeding appeared to have ceased. He had previously been unconscious for a few minutes. He was given $\frac{1}{4}$ gr. of morphia at once, which was repeated half an hour later, and after his clothes had been changed he fell asleep. At 9.30 a.m. the nurse reported his pulse to be hardly palpable, but when seen again at 11.30 a.m. he had quite a reasonably good pulse of 108, and his general condition was remarkably good considering the amount of blood which he had lost.

An aneurysm of the carotid artery at the base of the skull seemed the only possible explanation of such a profuse hæmorrhage, and this was confirmed by the presence of a blowing systolic bruit, audible over the right temple. There was no tinnitus. The decision was therefore come to to tie the external and internal carotid arteries on the right side immediately above the bifurcation, but it was thought advisable to wait until the infection of the upper respiratory tract had subsided. He was therefore kept as quiet as possible and given bromide and chloral, 10 gr. doses of each every four hours, and occasional doses of morphia hypodermically. During the next two or three days his general condition improved, in spite of the fact that he frequently coughed up small amounts of blood which was presumably leaking from the naso-pharynx.

October 4.—The systolic blowing murmur is now audible over the front of the head on both sides, slightly more pronounced on the right than the left. He complains, however, of very little headache and no throbbing. There is no evidence of any proptosis.

October 6.—Enema revealed old and fresh blood. Still some cough and catarrh of the upper respiratory passage. No recurrence of profuse hæmorrhage. Although extremely blanched his general condition is excellent. Pulse 80 to 88; temperature 98° F. to 100° F. 6 p.m. Blood examination. Red cells 1,950,000, hæmoglobin 35 per cent.; colour index 0.9, white cells 3,480, blood clots very slowly, very few blood-platelets seen in films; basophilic change in red cells well marked, with altered shapes and sizes, 3 normoblasts seen, polymorphs 56 per cent.; small lymphocytes 38 per cent., large lymphocytes 4 per cent.; large hyaline 2 per cent.

October 7.—1.0 a.m.: Another severe hæmorrhage from the nose lasting half an hour and treated with injections of morphia. In this attack he lost consciousness, the pulse jumped to 132, and it seemed extremely doubtful if he would survive 4.0 a.m. Condition very critical, but no further hæmorrhage. Pulse 120, extremely blanched. 5.0 p.m.: Operation under local anæsthesia, the right internal and external carotid arteries just above the bifurcation of the common carotid were tied by Mr. Wilfred Trotter. Prior to the operation the question of blood-transfusion was discussed, but owing to the great practical difficulties of carrying it out and the short time available, the idea was not persisted in. Moreover, the condition of the patient had gradually improved from the early hours of the morning throughout the day. At the moment of tying the vessels no changes were noticed in either pupil, nor was any weakness or reflex change produced in the limbs on the left side.

Note by Mr. Wilfred Trotter.—It is relevant here to state the reasons which led the surgeon to the choice of this operation. In general, it may be said that the surgical treatment of internal carotid aneurysms, intracranial or cervical, by proximal ligature, if it is unsuccessful fails through too little effect on the circulation rather than through too much. In dealing with these aneurysms the risk of doing an inadequate operation is greater than that of damaging the nutrition of the brain. There is in fact no condition which causes a more thorough dilatation of the collateral blood-supply of a part than does an aneurysm of its main artery. In this case there was a special reason for assurance that the collateral circulation was already fully prepared to nourish the brain. The primary hemiplegia was probably due to the peripheral end of the ruptured artery having been obstructed from the first, and yet it had passed off completely in a comparatively short time. It was to be presumed, therefore, that the left carotid was already chiefly answerable for the blood-supply of the anterior and middle cerebral territories on the right side.

The traditional treatment of internal carotid aneurysms is ligature of the common carotid. It is defective because it allows blood from the external carotid—freely supplied across the middle line of the face—to

pass down through the bifurcation into the internal carotid and so to reach the aneurysm. Ligature of the internal carotid itself, again, may be ineffective, because it allows blood to pass up the external carotid and through the orbit to the aneurysm. Clearly then two ligatures are necessary to give the fullest possible control of blood to the aneurysm. These may be applied to the two branches above the bifurcation, as was done in this case, or, as is sometimes more convenient, to the common and external carotids. A transverse incision with longitudinal splitting of the sterno-mastoid was used. It gives direct access to the vessels and avoids the permanent depression in the contour of the neck that is apt to follow the usual displacement of the muscle. The operation in itself is trivial, and this fact was felt to be an additional justification of its being done without preliminary blood-transfusion.

October 9.—General condition satisfactory. Temperature 102° F to 100° F. during the past forty-eight hours. Frequent harsh, dry cough and blood-stained mucus occasionally brought up. Nothing seen in the throat and no physical signs in the chest. Restlessness controlled by bromide and chloral.

October 11.—Temperature normal. Cough less frequent and mucus less blood-stained. The colour of the patient has improved. The movements of the right eye have definitely improved, but the right pupil is still wide and inactive. No further loss of vision or change in the right fundus as the result of tying the vessels. No sign of hemiplegia. The murmur over the skull remained unchanged. The patient was kept on a very limited diet and absolutely quiet for the next week, during which time his general condition continued to improve to a remarkable extent.

October 18.—Murmur over the right side of the skull much diminished and no longer audible on the left side. Ever since the last hæmorrhage there has been a rough systolic murmur audible at the apex and base of the heart. This is still present. The cough has disappeared. There has been no further sign of blood in mucus coughed up from the throat, and no recurrence of epistaxis.

October 22.—Further reduction of murmur over the right side of the skull; right temporal pulse barely palpable. Remarkable improvement in movements of the right eye, the only muscle which is now affected being the superior oblique. The left external rectus has also recovered. The left side of the face remains slightly weak.

November 5.—Excellent progress. His colour is returning and the general condition is excellent. Murmur over skull no longer audible.

December 7.—For the past fortnight he has been getting up, and for the past week has walked slowly out of doors for about twenty minutes each day. To day, when blowing his nose, he noticed two or three drops of blood on the handkerchief. Examination of the nose revealed some crusting rhinitis far forward, especially on the right side, and one or two small dilated septal vessels. These were sealed up with galvano-cautery, and were clearly the source of the hæmorrhage, which did not recur.

December 10.—Visual acuity in the right eye has now improved to $\frac{6}{8}$ (two letters). The right optic disc is paler than the left, but shows no other change. There is now no diplopia. The right pupil is rather large and does not react to light, but reacts to accommodation for the first time. The consensual reaction from right to left is positive, but from left to right negative. There is still slight infranuclear weakness of the left seventh nerve. No murmur is audible over the skull and the right temporal pulse cannot be felt. The anaemia is rapidly improving and he is now walking slowly for forty minutes a day. His mental condition is normal except that he has difficulty in making calculations, and is slower in the uptake than he was before the accident.

An X-ray of the skull shows a fracture running down the right parieto-temporal region, which loses itself at the base of the brain, no deformation of the sphenoidal sinus.

In *January, 1925*, he had a mild attack of influenza, from which he made a good recovery. At this time the vision in the right eye had improved to $\frac{6}{8}$, but beyond some pallor of the right optic disc and a slight contraction of the peripheral field of the right eye, the visual apparatus was normal. He could read with comfort for as long as he wished, and his general health showed no departure from the normal, beyond a difficulty in getting off to sleep before midnight.

On *March 16*, he was re-examined, with the following result: Colour normal. He can play a full round of golf and walk in hilly country without getting tired. Sleep normal. There is no difficulty in reading, and he has no diplopia. Visual acuity $\frac{6}{8}$ (four letters) right, $\frac{6}{8}$ left. The right optic disc is paler than the left, but the pallor is much less pronounced than it was. The vessels of the two fundi are equal and normal. No bruit over the skull; the right temporal pulse is absent. Mentally he feels he is still on the slow side in making calculations or reading difficult books; his memory is poor for recent events and he forgets trifles. He retains a very vivid recollection of the operation, but is not at all troubled by it. He has had no headache and no sign of epistaxis. The ocular movements are full. The right pupil is larger than the left and remains inactive to light, both direct and consensual; the reaction to accommodation-convergence is full. The left pupil reacts normally. There is slight contracture of the muscles round the left angle of the mouth. Otherwise there are no physical signs in the nervous system.

On *March 27* he sailed for Canada. Shortly after arrival he resumed his chemical studies at Toronto University, and his intellectual powers and general efficiency appeared to be in no way impaired by his illness.

After six months study he took up a business appointment and has been actively employed ever since. He enjoys excellent health and is not disabled in any kind of way. His vision, tested in January, 1928, is unaltered, viz., $\frac{6}{8}$ right, $\frac{6}{8}$ left, and the right optic disc is still somewhat pale. The right pupil remains inactive to direct light, but reacts slightly consensually. (Note communicated by Dr. Primrose.)

DISCUSSION OF DIAGNOSTIC POINTS.

In view of what happened after ligation of the carotids, viz., the immediate cessation of hæmorrhage and the more gradual disappearance of the localizing signs (paresis of the second, third, and fourth nerves), there can be little doubt that the essential lesion was an aneurysm of the intracranial carotid, the wall of which had given way and discharged its blood via the sphenoidal sinus into the nasal passages. The main object of this paper is to demonstrate that this diagnosis might have been made at a much earlier date and the risk of fatal hæmorrhage consequently obviated.

(1) *The initial hemiplegia.*—A complete flaccid left hemiplegia was noted immediately after the accident, while the patient was still unconscious. Within forty-eight hours consciousness was fully restored and power was rapidly returning in the paralysed limbs. A consideration of these facts provides a clue to the nature of the injury.

The possible causes of hemiplegia in fractures of the skull are : (1) Widespread laceration of the brain; (2) intracranial hæmorrhage, either extradural or subdural; and (3) unilateral cerebral anæmia. Apart from gunshot wounds, extensive cerebral laceration is always associated with gross external injuries and profound shock of long duration, neither of which conditions were present in this case. Again, hemiplegia is never an immediate result of subdural or extradural hæmorrhage, but develops after an interval of hours or days. It is invariably associated, moreover, with a return of coma if there has been a "lucid interval," or with an exaggeration of an existing coma, together with other signs of increasing cerebral compression. The course of events in this instance, however, was the very reverse, viz., an immediate hemiplegia with loss of consciousness, followed by a rapid return of consciousness and of recovery in the paralysed limbs. It would therefore appear that the most probable explanation of the hemiplegia was a unilateral cerebral anæmia, the result of a sudden obstruction of the circulation through the right internal carotid artery, and comparable with that which not infrequently follows ligation of the common carotid. This hypothesis is supported by the rapid disappearance of the paralysis during the first forty-eight hours, a period which coincided with a rise of arterial pressure from 100 mm. Hg to its normal level.

These considerations, together with the localizing signs supplied by the cranial nerve palsies on the side of the injury, point to the

probability that a laceration of the carotid in the neighbourhood of the cavernous sinus was sustained as an immediate result of the basal fracture, and that the arterial lesion, aided by the fall of blood-pressure, was primarily responsible for the ensuing cerebral anæmia.

The disappearance of the paralysis is to be attributed to the establishment of the collateral circulation through the circle of Willis rather than to any restoration of the blood-flow through the peripheral end of the damaged vessel; in fact, it is highly probable that the direct circulation beyond the wound in the artery ceased abruptly at the moment of injury and was never re-established.

(2) *Cranial nerve involvement.*—The cranial nerves involved were second, third, fourth, and to a less extent sixth, on the right, i.e., the side of the external injury, and sixth, seventh, and possibly eighth, on the left. The involvement of the nerves on the left side has no bearing on the arterial lesion, beyond the evidence it affords that the fracture followed the lines of the "typical" transverse fracture of the base, which passes across the body of the sphenoid in front of the dorsum sellæ and, turning backwards, loses itself in the region of the apex of the petrous bone of the opposite side.

Of the cranial nerve palsies on the right side, the most prominent and persistent was that of the oculomotor nerve. Immobility of the right pupil was noted on admission to hospital, and complete third nerve paralysis was found as soon as a more exact clinical examination was practicable. The paralysis was present in a less degree up to the time of the arterial ligature, after which it gradually disappeared, with the exception of a reflex iridoplegia which persisted. The trochlear nerve also was probably implicated from the outset, and paralysis of the superior oblique was certainly present up to the time of the ligature; nine weeks later no trace of it remained. The involvement of the abducent nerve was a more temporary affair, and the external rectus had completely recovered by the time the patient reached this country.

Of the nerves which traverse the cavernous sinus, the third and fourth stand in most intimate relation to the carotid, closely attached to its outer side and embedded, like the vessel, in the lateral wall of the sinus [1].

Moreover, in non-traumatic aneurysms of the third part of the internal carotid (i.e., within the sinus), paralysis of the oculomotor nerve is recognized as the most constant of the cranial nerve complications [2]. The sixth nerve is the innermost of the nerves traversing the sinus; it lies free in the sinus in the first part of its course forwards,

and finally passes obliquely across the sinus to become adherent to its lateral wall.

Except for transient right-sided headache immediately before the earlier attacks of epistaxis, no headache was complained of until nearly five months after the injury. The pain which then developed was referred to the right temporo-parietal region; it was never severe, and never associated with any demonstrable sensory disturbance in the area supplied by the trigeminal nerve.

The implication of the optic nerve is less easily explained, since it does not transverse the sinus. It will be remembered that the carotid

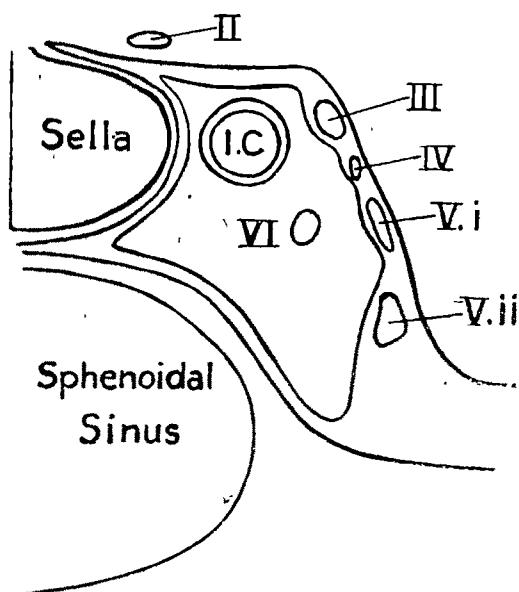


FIG. 1.—Coronal section through the middle of the cavernous sinus (diagrammatic).

artery, before entering upon the fourth part of its course, bends upwards and escapes from the cavernous sinus by piercing the inner layer of the dura mater which forms its roof. The ophthalmic artery is given off just after the emergence of the main vessel from the sinus, although exceptionally it arises within the sinus. The carotid, lying now in direct relation with the base of the brain, turns abruptly backwards and outwards beneath the optic nerve to the outer side of the chiasma. Involvement of the optic nerve at the chiasma, as might be expected on anatomical grounds, is a well-known feature of "spontaneous" aneurysms of the fourth or

but not of its third part, and various considerations render it impossible for the laceration of the vessel to have occurred in this case distal to the origin of the ophthalmic artery. In other words, we have here to account for a disturbance of function of the second nerve associated with an arterial injury which must have been sustained by some part of the vessel as it traverses the sinus, and the three following explanations suggest themselves. In the first place, it is conceivable, that the visual disturbance bore no direct relation to the carotid lesion, and was brought about by the involvement of the optic foramen in the fracture. In support of this view Hewett [4] found that out of 68 cases of fractured base examined after death the orbital roof was broken in one-third, while in 84 cases of fractured base investigated by von Hölder [5] the orbital roof was involved in 79, and the upper wall of the optic canal was fissured, or fractured, in 63, of which 42 had bleeding into the sheath of the optic nerve. On the other hand, it is generally recognized that with very few exceptions fracture through the optic foramen leads to complete and permanent loss of vision on the side of the injury. In this connection it must be remembered that the optic foramen is a crowded thoroughfare, and that the nerve is embedded in the sheath of the ophthalmic artery and firmly fixed thereby to the walls of the canal, particularly the upper wall [1]. Further, the early pallor observed in this case without gross loss of visual acuity is not at all suggestive of a primary involvement of the nerve in a radiating fracture, while the recovery of vision and the reduction of the pallor after tying the carotids make it much more probable that the arterial lesion within the skull was directly related to the visual disturbance.

Secondly, it is possible that the optic nerve was compressed by the blood extravasated at the time of the injury. This in fact was probably the case, but as the clot became absorbed the disturbance of visual function should have diminished, whereas the evidence tends to show rather that it increased, since by the time the patient arrived in this country, four months after the accident, he was well aware of considerable loss of vision in the right eye. Moreover, on anatomical grounds it is difficult to ascribe this progressive loss of vision to compression of the nerve by an aneurysm of the third part of the carotid, since in this part of its course the artery is some distance away from the nerve.

The third possibility is that the visual phenomena were not due to actual compression of the optic nerve, but were merely an expression of a severe retinal anæmia caused by interference with the ocular blood-

supply resulting from an aneurysm of the carotid in the neighbourhood of the origin of the ophthalmic artery. The question whether a retinal anæmia, such as is here assumed, could give rise to the disturbances met with in this case is discussed in a later section. It is conceivable that an arterial hæmatoma might compress the wounded carotid itself, as well as the ophthalmic artery, sufficiently to obstruct very considerably the arterial supply to the eye, and that the aneurysm, while having a similar compressive effect, might also act as a lake and thereby lower the blood-pressure in the distal part of the parent vessel and its branches.

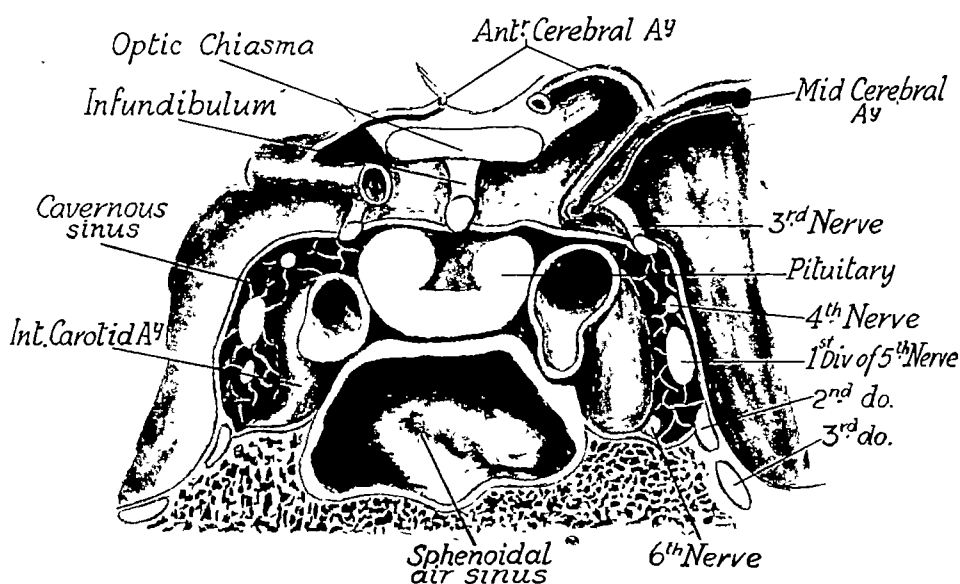


FIG. 2.—Coronal section through the pituitary body. Scale drawing from a specimen in the Anatomical Department, St. Thomas's Hospital. (Prof. F. G. Parsons.)

Certain obvious objections, however, attach to this hypothesis. In the first place, it places the carotid lesion outside the sinus, and therefore renders the involvement of the third, fourth and sixth nerves unintelligible, while secondly it fails to explain the rapid recovery of vision which ensued after ligature of the vessels, together with the more persistent pallor of the disc. For it is evident that, if the recovery of vision was due solely to increased blood-flow along the ophthalmic artery, the retinal pallor should have undergone a proportional improvement. The theory of retinal anæmia, therefore, as being solely responsible for the condition, cannot be sustained.

None of the hypotheses above discussed afford a wholly satisfactory

interpretation of the facts observed, and the most reasonable explanation would appear to be that the hæmatoma and succeeding aneurysm were not in direct relation to the nerve, but that the pulsations of the aneurysm within the boundaries of the cavernous sinus were transmitted to the more distal part of the carotid, and so compressed the nerve from below upwards against the upper wall of the optic foramen. It is highly probable that the ophthalmic vessels also suffered compression in the same way, and the relative retinal anæmia so produced may account for the pronounced pallor of the disc without obvious impairment of vision which was observed as early as six weeks after the injury, that is to say, at a time when gross ophthalmological changes as a result of a lesion of the nerve at the optic foramen could hardly have been expected. Absence of venous congestion of the globe and retina does not militate against this hypothesis, owing to the communications other than with the cavernous sinus which are still open to the venous return, namely, forwards, via the angular vein into the facial system, and downwards through the inferior orbital fissure into the pterygoid venous plexus. As the aneurysm slowly expanded the increasing pressure thus indirectly exerted on both nerve and vessels led to a progressive impairment of visual acuity, which eventually fell to $\frac{6}{17}$. Ligature of the carotids by cutting off the whole or the greater part of the circulation through the sac relieved the compression, and was followed by the restoration of conduction in the nerve fibres, except for a small number in which the damage was permanent, as manifested by the clinical condition six months after the operation, viz., visual acuity $\frac{6}{9}$, and slight pallor of the disc, a condition which has persisted unaltered ever since.

Many considerations, and more particularly the cranial nerve palsies and attacks of epistaxis, render it inconceivable that the carotid can have been torn after it had emerged from the cavernous sinus, and therefore beyond the origin of the ophthalmic artery.

(3) *Epistaxis*.—Profuse and uncontrollable hæmorrhage from the nose and mouth is recognized as an immediate and fatal accompaniment of fractures of the base of the skull with rupture or laceration of the internal carotid artery or arteries. The relations of the sphenoidal sinus to the middle fossa and of the upper nasal passages to the floor of the anterior fossa render this phenomenon readily intelligible. It is therefore all the more curious that no example of epistaxis occurring as a late result of intracranial aneurysm, either traumatic or non-traumatic, appears to have been recorded.

It has already been pointed out that the paralysis of the left sixth

and seventh nerves is evidence of the fracture having passed from right to left across the body of the sphenoid which forms the roof of the sphenoidal sinus. No epistaxis is known to have occurred until six weeks after the original injury, although prior to that the patient had observed that the mucus coughed up on waking was blood-stained. The attacks of epistaxis gradually increased in frequency and violence, and finally culminated in a series of hæmorrhages so sudden and profuse that any one of them might have proved fatal to an individual endowed with a less vigorous constitution. In these latter attacks the blood was always arterial, and flowed in a steady continuous stream from both nostrils. Such a train of events is obviously compatible with aneurysmal "weeping" in the earlier, and with rupture of the sac in the later, stages. Presumably the aneurysm eroded the thin roof of the sphenoidal sinus, and the headache experienced in the later stages may be thus explained.

An error was committed in paying insufficient attention to the results of the blood examination made some days before the final attacks of epistaxis. Although the red cell-count was normal, nearly 5,500,000, the hæmoglobin percentage had fallen to 79, giving a colour index of 0·7. Moreover, the red cells presented well-marked basophilic changes and other signs of immaturity, signifying the efforts of the bone-marrow to compensate for a serious draining away of erythrocytes from the circulation.

(4) *The arterial bruit*.—In practically all cases of pulsating exophthalmos secondary to an arterio-venous aneurysm, a loud venous hum is audible both to the auscultator and the patient. On the other hand, out of 44 cases of non-traumatic arterial aneurysm of the cerebral vessels collected by Fearnside, noises in the head were complained of in one case only; auscultation of the skull was apparently not practised. In the present case no bruit was audible four and a half months after the injury, and it was heard for the first time four weeks later and immediately after the last hæmorrhage but one preceding the tying of the carotids. At no time was it very loud, and tinnitus was never complained of, although the patient was frequently interrogated on the point. Tying the vessels did not immediately abolish the bruit, which gradually faded away until four weeks later it had disappeared. The bruit was not transmitted to the heart, and was always louder on the side of the lesion, and at times confined to that side. The slowness of its fading was probably due to the fact that a certain amount of blood continued to reach the aneurysm via the circle of Willis, and its

final disappearance may be regarded as coinciding with progressive thrombosis within the aneurysm, leading to progressive organization and shrinkage of the sac.

The whole question of local vascular murmurs in gunshot injuries of the blood-vessels has recently been dealt with by Makins [6], who states that "the existence of an intracranial injury to the internal carotid may usually be determined by auscultation of the skull, when the characteristic systolic bruit, or an arterio-venous murmur, will be audible." He quotes no examples, however, of such intracranial injuries, but refers to a case in which the absence of such a murmur led to a correct diagnosis.

The site of the carotid lesion.—In the previous section the arguments in favour of the view that the carotid was lacerated in the third part of its course as it passes forward in the lateral wall of the cavernous sinus at the side of the body of the sphenoid, have been discussed. The implication of the third and fourth nerves, the more transient paralysis of the sixth, and the attacks of epistaxis all accord with this hypothesis. An explanation of the involvement of the less intimately related optic nerve has been put forward, and reasons have been given to show that the injury of the vessel must have been at some point proximal to the origin of the ophthalmic artery. These various considerations render it probable that the artery was injured in the latter part of its course through the cavernous sinus, but definitely before its exit. The comparative rarity of injury to the vessel in fractures of the basis cranii is presumably due to the elasticity of its walls and its freedom within the bony canal which it traverses. In the cavernous sinus the artery is to some extent anchored by the dura mater, which it pierces both on entering and leaving the sinus, but this anchorage is to a large extent nullified by the right-angled bend taken by the vessel, which permits it to pass out of the sinus by piercing its roof.

The absence in this case of any communication between the artery and the sinus is one of its most curious features. One can merely assume that the laceration was situated on the inferior aspect of the vessel, and that the resulting aneurysm expanded in this direction and so into the sphenoidal sinus. Why this does not happen more frequently it is impossible to say.

The nature of the arterial lesion.—Wounds of arteries are usually classified as contusions or lacerations, and the experience of the War demonstrated that the former, as well as the latter, may lead to the formation of aneurysms. The precise nature of the lesion cannot of

course be determined in the present instance, but since contusions are particularly apt to lead to a rapidly-spreading thrombosis, a condition which in this case can be negatived on clinical grounds, and since the carotid injury was associated with an extensive fracture of the base of the skull, it may be taken for granted that the vessel was actually lacerated by a bone fragment. The subsequent clinical history is entirely compatible with what is known to be the common sequence of such lateral wounds of arteries, viz., the development of an arterial hæmatoma and subsequently of an aneurysm. The extent of the hæmatoma and its line of extension is determined in any given case by the size of the artery, the severity of the laceration, the support afforded by the surrounding structures, and the anatomy of the region. In injuries such as the one under discussion, support is provided by the dura and the skull case and their attachments to one another. In this manner hæmatomata in basal fractures tend to remain localized and to become rather rapidly converted into a firm clot, which in this case by the pressure it exerted on the main vessel may have helped to control the bleeding.

The process by which an arterial hæmatoma is converted into an aneurysm is essentially twofold [7], first the contraction of the coagulum, and secondly the reaction induced in the surrounding tissues. As regards the former, the impact of the blood-stream opposite the defect in the arterial wall tends to hollow out a rounded space in the recently coagulated blood, and the resulting cavity acquires a boundary formed by the disposition of well-marked layers of laminated clot resembling that met with in typical spontaneous aneurysms. At a relatively early stage the sac, when laid open, presents a smooth shining surface, representing a distinctly new formation, quite independent of, and bearing little relation in size or structure to, the primary blood-clot. The reaction of the surrounding tissues to the stimulus afforded by the clot is energetic from the outset and is partly responsible for its absorption. As seen in a limb, the connective tissue of the vascular cleft, the intramuscular spaces, and the muscles themselves become infiltrated with serum and an abundance of leucocytes. The induration thus induced affords support to the original clot and tends to prevent the wider extension of the aneurysm. At the base of the brain the only reactive tissues are the dura mater and its extensions, and these are not particularly endowed with the property of vigorous local reaction at all comparable with that possessed by the soft tissues of a limb, although to neural stimuli they are known to respond with remarkable energy.

It must further be remembered that the pressure arrangements within the rigid skull are equally unfavourable both to the rapid extension of bleeding and also to the absorption of any clot which may have formed. It would therefore appear that at the base of the skull the limits of an arterial hæmatoma, and the size and direction assumed by any subsequent aneurysm, are governed mainly by mechanical and anatomical considerations, and that the reaction of neighbouring tissues is of less importance than in other parts of the body.

A NOTE ON THE EFFECTS OF OBSTRUCTION OF THE CAROTID CIRCULATION ON THE HOMOLATERAL EYE.

In the case here described the question arose as to whether interference of the ocular blood-supply as a result of obstruction of the intracranial carotid could have been a principal or subsidiary factor in the production of the visual disturbances observed, namely, pallor of the disc, slight constriction of the fields, and progressive impairment of acuity. It was evident that, provided the circulation through the circle of Willis was effective and the origin of the ophthalmic artery was not involved in the lesion of the parent vessel, no interference with the ocular circulation was to be expected. On the other hand, it was recognized that hemiplegia or monoplegia is a not infrequent consequence of ligature of the internal or common carotid, and in the present case a complete but transitory hemiplegia had been a conspicuous feature in the earliest stages. Seeing, then, that obstruction of the internal carotid from any cause is apt to be followed by gross cerebral manifestations, it did not seem unreasonable to speculate on the possibility of the ophthalmic circulation also suffering in sufficient degree to give rise to some impairment of vision, provided this was particularly looked for. No such disturbance of vision is, however, mentioned in any textbook of surgery to which the writer has had access, and although the presumption is, therefore, that such disturbances do not occur, the matter seems of sufficient interest to warrant a brief note. The question may be considered from the anatomical, clinical, and experimental standpoints.

I. *Anatomical*.—The blood-supply of the human eye is derived almost entirely from the ophthalmic artery, i.e., from the intracranial portion of the internal carotid. The only vessels with which the branches of the ophthalmic artery anastomose are those of the external

carotid, and these communications, as judged by descriptions in text-books of anatomy, are neither numerous nor large (see footnote).¹

As regards their collateral circulation, therefore, the ocular and cerebral blood-supplies appear to be on the same anatomical footing and dependent primarily on the efficiency of the circle of Willis, while on anatomical grounds it is justifiable to suppose that ligation of the ophthalmic artery would, altogether apart from the possibility of spreading thrombosis or embolism, render the eye bloodless and sightless. The terminal branches of the vessels originating from the external carotid of the two sides anastomose freely with one another across the middle line.

II. *Clinical.*

(A) General conditions capable of producing retinal anæmia.

The anæmias: Disturbances of vision in anæmic states may obviously be of central (cerebral) or peripheral (retinal) origin, while a further difficulty is presented by the fact that the changes occurring in the brain or retina may be due, not to the anæmia itself but to the causes which provoke it, as well as to the general bodily disturbances engendered by it. Such conditions, therefore, as retinal hæmorrhages, venous thrombosis, the so-called optic neuritis of chlorosis [8], and so on, may be eliminated from the present argument, seeing that they are themselves productive of disturbance of vision apart from the associated retinal anæmia.

In chlorosis constriction of the visual fields has been observed by Groenouw [9], and various ophthalmoscopic changes relative to the appearance of the retinal vessels have been described, none of which are characteristic or necessarily associated with impairment of vision. In pernicious anæmia, the writer has never seen demonstrable loss of vision apart from widespread retinal hæmorrhages. After serious loss of blood, visual disturbances are common, and in some cases their peripheral

¹ The following list of the anastomoses between branches of the ophthalmic and external carotid arteries is compiled from Cunningham's "Textbook of Anatomy": (1) Posterior ciliary; (2) central artery of the retina; (3) recurrent; (4) ethmoidal; (5) frontal; (6) muscular—none mentioned; (7) lachrymal—with orbital branch of middle meningeal, with orbital and anterior temporal branches of superficial temporal, with deep temporal branches of internal maxillary; (8) palpebral—with infra-orbital branch of internal maxillary, with angular branch of facial, with orbital and anterior temporal branches of superficial temporal; (9) supra-orbital—with anterior terminal branch of superficial temporal; (10) nasal—with angular and lateral nasal branches of facial. In addition, the anterior ciliary branches of the lachrymal anastomose with the posterior ciliary vessels, while the muscular, supra-orbital, palpebral and frontal branches anastomose with each other to a small extent.

origin is suggested by the fact that they are at times unilateral and accompanied by early changes in the fundus oculi [10].

In quinine, and to a less extent tobacco, amblyopia, the clinical and experimental evidence is in favour of the view that the loss of vision is the result of a general constriction of the retinal arteries with consequent retinal anæmia.

(B) Local conditions capable of producing retinal anæmia.

(1) In certain cases in which compression of the carotid has been undertaken, slight alterations in the filling of the vessels of the retina have been observed, but the changes are inconstant. It should also be remembered that the cervical sympathetic is likely to be included in the compression.

(2) Transient blanching of the optic disc has been observed to coincide with the tightening of a ligature round the common carotid [11].

(3) Ligature of the common or internal carotid is the recognized treatment for pulsating exophthalmos associated with arterio-venous aneurysm. The results as regards the eye condition are somewhat uncertain, but when beneficial may be ascribed to the reduction of venous pressure in the cavernous sinus and ophthalmic veins consequent on the diminution of arterial blood-supply to the aneurysm. Cerebral complications are by no means infrequent, and the mortality of the operation ranges from 10 per cent. (de Schweinitz) [12] to 6 per cent. (de Fourmestaux) [13].

(4) Siegrist [14] collected from the literature 997 cases in which the carotid had been ligatured for a very great variety of pathological conditions. In eight cases considerable blindness of the homolateral eye followed, but in six of these sepsis, thrombosis, or embolism were probably responsible. Of the remaining two cases, in one the left common carotid was tied on account of hæmorrhage from a gunshot wound of the upper jaw; the operation was followed by no cerebral complications but by diminution of vision of the left eye, left-sided deafness, and symptoms of paresis of the left vagus. There were no ophthalmoscopic changes, and after three years the vision had improved. In the second case the right common carotid was tied on account of hæmorrhage from a telangiectatic tumour of the scalp; as the ligature was tightened the patient became blind in the right eye. There were no cerebral symptoms, and the vision returned three days later, but remained misty up to the time of death seven years afterwards.

In fourteen cases out of 997 fleeting visual disturbances occurred, but in only two of these cases were there any cerebral phenomena. In three cases (hæmorrhage from tumour of the nostril, cirroid aneurysm of the jaw, and nævus of the ear) both common carotids were tied at intervals ranging from three weeks to some months. In one case each ligature was associated with transient dimness of vision in the homolateral eye without cerebral symptoms, while in the other two the second ligature was followed by complete blindness of the homolateral eye which persisted for half an hour in one case, and by more temporary impairment of vision in the other. In neither case was there any cerebral disturbance.

Generally speaking, the visual disturbances in these fourteen cases were of the nature of retinal syncope.

Gross cerebral symptoms were a frequent complication in the 997 cases, and the mortality was 38 per cent.

(5) Makins [15] has recently drawn attention to the haphazard incidence and irregular nature of the cerebral complications associated with gunshot wounds of the vessels of the neck and their surgical treatment. Of twenty-seven cases in which the common carotid was ligatured for wounds, hemiplegia occurred in eight (29.6 per cent) with a mortality of 11.1 per cent, but in none of these cases is there any mention of visual disturbance. The fundus oculi was examined in a number of men whose common carotid had been tied fourteen to twenty-one days previously with negative results, but it is not stated whether cerebral symptoms were present in these cases or not.

III. *Experimental.*

(i) Injection of vessels. Elschnig [16] showed that with low pressures (60 cm. of water), when in the cadaver the ophthalmic artery was divided from the internal carotid and the latter tied, fluid injected into the external carotid or internal maxillary artery of the same side could be seen to flow from the cut ophthalmic artery in a relatively short time, and that finally both orbits and both sides of the face were filled with the injection fluid. He concluded that the ocular blood-supply must be in part derived from the external carotid, the branches of which communicate freely on both sides.

(ii) Animal Experiments. It has been pointed out by Parsons [17] that the blood-supply of the orbit in the lower mammals is derived almost entirely from the external carotid, and that as we ascend the animal scale the general tendency is for the principal ophthalmic artery

to be derived more and more from the internal carotid. In the dog there is a large anastomotic branch from the internal carotid within the skull which usually joins the internal maxillary artery just before the ophthalmic artery or arteries are given off from that vessel. Ligature of the external carotid in the dog, therefore, cuts off the main blood-supply to the eye, and such an operation is followed by a fall of intra-ocular pressure which lasts for some time, but the eye is still sufficiently supplied with blood through the internal carotid and through the circle of Willis by the anastomotic branch.

Schulten [18] observed a fall of intra-ocular tension in rabbits after carotid ligature. Michel [19] found no evidence of gross visual disturbance in dogs after bilateral carotid (? which) ligature. Wessely [20], reviewing the subject, regards the fall of intra-ocular pressure and diminution of aqueous production as the characteristic consequences of a unilateral ligature, together with pallor of the eye, and states that, whereas in cats and dogs these phenomena persist for two or three weeks, in the ape conditions are restored to normal much more quickly.

The effects of carotid ligature on the intra-ocular tension in man have not, so far as can be ascertained, been investigated.

Before commenting on these facts, it is essential to point out that the cerebral and ocular disturbances after carotid ligature may be, and in fact in a majority of cases probably are, attributable to the pathological conditions for the relief of which ligature has been undertaken, such as severe hæmorrhage, sepsis, toxæmia from malignant disease, arterial degeneration, and so on. Moreover, ligature of the vessels is apt to be followed by a rapidly-spreading thrombosis, which may extend throughout the distal portion of the vessel and into its branches, while a further danger is the possibility of emboli arising from the local clot at the site of the ligature or from the extending conglulum above referred to. Bearing this in mind, the conclusion appears to be justified that, in the absence of spreading thrombosis or embolism, unilateral ligature of the common carotid in man, with very few exceptions, is productive of no demonstrable disturbance of vision apart from occasional transient and fleeting phenomena, whereas the operation is associated in a considerable number of cases with gross cerebral disturbance which may or may not be permanent.

This striking difference in behaviour might be ascribed to the greater vulnerability of the brain to sudden interference with its blood-supply, and it is probably true that the retina can tolerate such inter-

ference over a longer period than the cerebrum without suffering any permanent damage. But if this were the only explanation, one would expect obvious cerebral disturbances to be invariably associated with ocular symptoms in those cases in which the latter manifest themselves after the carotid ligature; such a correlation, however, has not been established, and the two sets of phenomena seem to be independent of one another. Another factor which might account for the anomalous behaviour of brain and eye is an essential difference in the nature of their collateral circulations, but for such a difference there is, apart from the experience of clinical surgery, little direct evidence, since with the exception of Elschmig's injection experiments and certain ocular complications met with after paraffin injections for the relief of sunken noses, the anatomical evidence is rather in favour of the view that the collateral circulations are similar and dependent in each case on the efficiency of the circle of Willis. This view is clearly expressed in textbooks of ophthalmology: "The ophthalmic artery has very few and insignificant anastomoses, so that on the arterial side the ocular circulation is an offshoot of the intracranial circulation" [21]. It may be, however, that the anatomical evidence is deceptive, and that the anastomoses between the territories of the ophthalmic and external carotid arteries, however small and insignificant they may appear in the cadaver may, in cases where the direct blood-supply is obstructed, be capable of supporting a vigorous collateral circulation and thus of assuming considerable clinical importance. If this be so, and taking into consideration the free and extensive anastomosis across the middle line between the branches of the external carotids, it is easy to understand how, after ligature of the common carotid or of its two main branches, the orbit can still be adequately supplied with blood independently of the intervention of the circle of Willis.

It is a pleasure to acknowledge the assistance of those who contributed by their advice and skill to the successful outcome of this case. More particularly am I indebted to Mr. Wilfred Trotter for his technical skill and wise counsel, both in the care of the patient and in the preparation of this paper; to Professor F. G. Parsons for the drawing which accompanies it and for his help in connection with certain anatomical aspects; and lastly, to Dr. A. Primrose and his colleagues at the Toronto General Hospital for kindly supplying me with full notes of the early phases of the case.

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THE CENTRAL NERVOUS CONTROL OF MICTURITION.¹

BY F. J. F. BARRINGTON.

MICTURITION can be artificially produced by slowly injecting warm water into the bladder; when a certain distention is obtained the bladder reacts, expelling the water. It was found by Guyon [11], in curarized dogs, that this reaction is not altered by division of the hypogastric or of the pudic nerves, and therefore must depend on the integrity of the pelvic nerves which were then the only pair remaining. He confirmed this by showing that it was abolished by division of the pelvic nerves. If this experiment is performed on female cats under ether, by passing a catheter and gradually distending the bladder through it, the reaction is found to take place, some lotion being expelled by the side of the catheter, but generally an appreciable, and frequently a large, fraction of the lotion remains in the bladder at the end of the reaction. If a cat is decerebrated under chloroform, and then allowed to come out of the anæsthetic and the same experiment performed, the fraction of the water left in the bladder after the reaction is inconsiderable and not more than could be accounted for by the mechanical obstruction produced by the catheter. The reaction is abolished by division of both pelvic nerves or by transection of the spinal cord [1].

If a catheter is tied into the urethra of a decerebrate cat without any exposure of the bladder, and a continuous record of the bladder volume under a constant pressure of 10 cm. of water is taken, the volume shows rhythmic contractions which are generally very sharp, suggesting that they are reflex. Division of the spinal cord or of both pelvic nerves abolishes these contractions and leads to a permanent increase in the bladder volume. The same effect is produced, though less rapidly, by the administration of chloroform or ether. There therefore appears no doubt that the rhythmic contractions seen in the volume are in fact reflex contractions due to distention of the bladder. To determine the level of this reflex in the central nervous axis, it is

¹ The seventh Sydney Ringer Memorial Lecture, delivered at University College Hospital Medical School, on February 24, 1928.

only necessary to make transections at various levels and observe the effect on the bladder volume. In making such experiments it is necessary to exclude the violent movements which take place in the part of the animal distal to the transection by previous injection of curare, otherwise the contractions of the trunk muscles affect the volume of the bladder. Curare dissolved in acidified Ringer's solution, when injected intravenously, itself produces a similar effect on the bladder volume to chloroform, ether, division of the pelvic nerves, or transection of the spinal cord, but if given in appropriate doses subcutaneously, the contractions of the bladder remain, though its volume is rather increased,

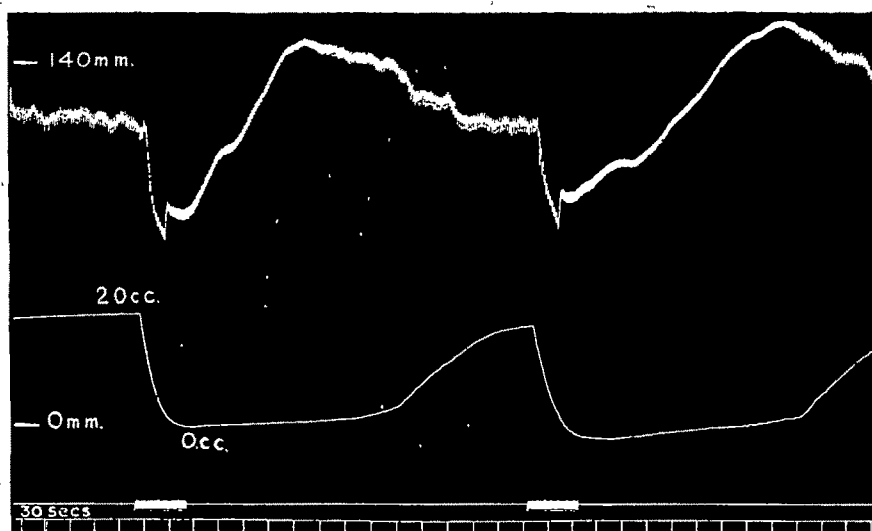


FIG 1.—Cat. Ether. Tracheotomy. Vagus and pelvic nerves on each side divided. Carotid blood-pressure and bladder volume at 10 cm. of water pressure. No ether had been given for seven minutes before the beginning of the tracing, and none was given during the tracing, except during the signals; then the whole inspired air came through a Wolff's bottle of ether.

while the effect on the skeletal muscles is sufficient for the purpose. In this way it was found that transections behind a plane through the posterior parts of the inferior colliculi dorsally, and the middle of the pons ventrally, always led to abolition of the contractions and to a permanent increase in the volume, while transections in front of this plane either did not affect the volume or the effect was only transitory. It may therefore be concluded that the reflex contraction of the bladder which occurs through the pelvic nerves, as a result of its own distention, arises in the central nervous system at about the level of the plane

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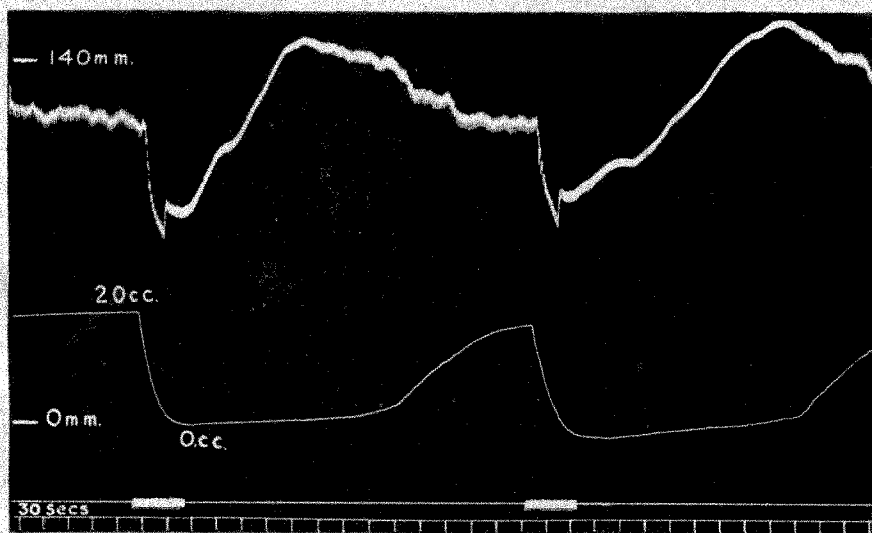


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through the posterior parts of the inferior colliculi dorsally and the middle of the pons ventrally [3].

The effect of ether on the bladder volume of an intact cat differs from that described in a decerebrate cat. In an intact cat under ether the effect of increasing the ether is a contraction following a latent period of six to eleven seconds, which is associated with a fall of arterial blood-pressure. Should the cat hold its breath after the contraction has started, the contraction ceases and begins again when respiration is renewed. This is not an effect on the nervous mechanism of the bladder, since it occurs if both pairs of nerves to the bladder are divided. It also occurs after the spinal cord has been transected, the vagi or splanchnic nerves divided on both sides, or if the suprarenals or pituitary have been removed a few minutes previously.

The best method for examination of the reflexes which make up micturition is to observe the bladder pressure and urethral resistance simultaneously under conditions which can be varied at will. This was done on decerebrate cats which had come round from the anaesthetic. It is preferable, but not necessary, to use females. A median suprapubic incision was made, the ventral surface of the junction of the bladder and urethra exposed and divided, and a cannula tied into each cut end. Each cannula was connected with a warm water manometer which could be filled from a reservoir. In this way five separate reflexes were found, the first two of which led to a powerful contraction of the bladder.

The first reflex was the one already described by Guyon. If the bladder volume was increased by small amounts at regular intervals of time, a certain volume was found, which was more or less constant for each individual but varied widely in different individuals, at which the bladder pressure suddenly rose 40 to over 90 cm. of water. The pressure which excited this contraction was always less than 10 cm. of water. The reflex persisted after division of the hypogastric or of the pudic nerves, but was abolished by division of the pelvic nerves, transection of the spinal cord, or by cocainizing the interior of the bladder. The reflex must therefore arise in the brain, and have both its afferent and efferent paths in the pelvic nerves. It is evident that the pressure and not the volume is the essential factor in evoking this reflex, since the volume which excites it is only constant so long as the volume increments are made at the same rate, a diminished volume evoking the reflex if the rate of increase of volume is increased. Mosso and Pellacani [16] were the first to show that the intravesical pressure and

not the volume is the determining factor in causing the micturition reflex. They used a bitch which could be repeatedly catheterized without evincing signs of annoyance. They emptied the bladder and then gradually filled it with warm water at pressures gradually increasing by 5 cm. of water, allowing four minutes to elapse between each increment. It was found that the bitch always became restless at 20 cm. of water pressure, though in different experiments the bladder contained very varying volumes at this pressure.

The second way in which a strong reflex contraction of the bladder could be evoked was by running water through the urethra. It was demonstrated by putting a volume of water into the bladder insufficient to evoke the first reflex, and then gradually raising the pressure in the urethra manometer until the urethral resistance was overcome and water escaped from the external meatus. The bladder pressure rose to about the same extent as in the first reflex, after a latent period of about two seconds. This reflex could be obtained after division of the hypogastric nerves or after cocainizing the bladder interior, but not after division of the pelvic nerves. In nine experiments the pudic nerves were divided, the pelvic and hypogastric nerves being intact; in eight of these the reflex was abolished, but in the remaining one it persisted and was subsequently abolished by division of the hypogastric nerves. This reflex, like the last, therefore arises in the brain and has its efferent path in the pelvic nerves; the afferent path appears to be, at any rate usually, in the pudic nerves.

The third reflex that excites a bladder contraction differed from the first two in that the contraction was very transient and relatively slight, the pressure rise varying from 3 to 15 cm. of water instead of from 40 to over 90 cm. It resulted from distension of the proximal part of the urethra and was demonstrated, after division of both pelvic nerves, by gradually raising the pressure in the urethra manometer. After a certain elevation of pressure, a sudden slight fall of the level of the manometer was observed without any escape of water from the meatus, showing that the volume of the urethra had increased. The bladder contraction always followed this fall. It was not abolished by division of the pudic nerves or by transection of the cord, but was abolished by division of the hypogastric nerves. The reflex therefore arose in the cord, and both its paths were in the hypogastric nerves.

The two remaining reflexes led to relaxation of the urethra. The fourth was evoked by running water through the urethra when the bladder was empty or only contained a small volume. The water in

the urethra manometer was slowly raised. When a certain pressure, which was fairly constant in the same individual, was reached, water escaped from the meatus and the pressure fell quickly to a much lower level, which was also fairly constant in the same individual. As intermediate pressures were not resisted by the urethra during the flow of water, and were resisted while the pressure was being raised, the urethra must be reflexly relaxed during the flow. Division of both hypogastric nerves does not affect this reflex. After division of both pudic nerves water escapes from the external meatus at a much lower pressure than previously, and after the escape has led to a sufficient fall of pressure to stop the flow, the slightest increase of pressure starts it again; division of both pudic nerves, therefore, abolishes the reflex. After division of both pelvic nerves or transection of the spinal cord, the pressure which the urethra resisted increased; when the escape of water took place it did so in a series of jets which took longer than the continuous flow previously seen, and the fall in the pressure was usually not so great. Manifestations of this reflex were therefore not abolished by division of the pelvic nerves or transection of the spinal cord, but they are altered by these. The alteration is probably due to the abolition of the reflex bladder contraction which increases the effect of this reflex by means of the fifth reflex. The fourth reflex is therefore situated in the spinal cord and has both its paths in the pudic nerves.

In the fifth reflex distention of the bladder produces relaxation of the urethra. The urethra manometer was filled to a pressure intermediate between that which was previously found to lead to escape of water from the meatus, and that to which it fell after the escape started. The bladder was then slowly filled as before, by running in equal volumes at equal intervals of time. It was found that when the reactionary rise of intravesical pressure occurred through the first reflex, water escaped from the external meatus and the pressure in the urethra manometer rapidly fell. The reflex was abolished by division of both pelvic nerves, or by cocaineizing the bladder interior, and was unaffected by division of the hypogastric nerves. After division of the pudic nerves no effect could be produced on the urethral resistance remaining by distension of the bladder. Spinal transection did not abolish the reflex. After this operation the bladder volume which had previously caused the bladder contraction and urethral relaxation had no effect on either except when the volume of the bladder was greatly increased, leading to a marked increase in intravesical pressure, water escaped from the meatus and the pressure of the urethra manometer fell in

consequence. If, after spinal transection, the urethra manometer was gradually filled and the pressure at which escape of water occurred was measured at various intravesical pressures, it was found that the greater the intravesical pressure the lower the pressure at which the escape of water from the meatus started. The fifth reflex is therefore situated in the cord, has its afferent path in the pelvic nerves and its efferent in the pudic nerves.

There is no function more obviously under the direct control of the will than micturition. The existence of the five reflexes just described shows that it does not necessarily follow from this that contraction of the bladder is directly under the control of the will. Any one of the reflexes, with the possible exception of the third, can bring all the others into action. In the second reflex the bladder contraction was produced by running water through the urethra, but there was nothing in the observation to show that the water in the urethra was the real stimulus to bladder contraction; if, instead, the real stimulus is the inhibition of the compressor urethræ produced through the fourth reflex by water running through the urethra, voluntary micturition could be produced by action on a striped muscle without any direct action on the bladder.

In both man and the cat urine is held at the internal meatus, and the part of the urethra between this and the compressor urethræ only contains urine during micturition. This can be shown in man by passing a catheter with the opening at the end, when it is found that the distance the catheter has to be pushed in, after it has been felt to pass the compressor urethræ, until urine escapes corresponds to the length of the prostatic urethra. In man it is known that the compressor urethræ is capable of holding urine when the urethra proximal to it has been destroyed by the operation of suprapubic prostatectomy [17]. It was found by Griffiths [10] that division of the urethra between the prostate and the bladder did not lead to the escape of urine in an anæsthetized cat, even when the bladder was full. In both man and the cat the closure of the proximal part of the urethra can be shown by taking an X-ray after filling the bladder with some opaque fluid. Courtade and Guyon [5] found that the pressure necessary to force water back into the bladder of a dog was at least five times greater when it had to be forced through the compressor urethræ and prostatic urethra than when it had to be forced through the prostatic urethra only. That the compressor urethræ is contracted more strongly than the prostatic urethra in man can be felt when a catheter is passed. Therefore, though urine is normally held by the closure of the urethra

proximal to the compressor urethræ, it can be held by the compressor urethræ, and this part of the urethra, though further from the bladder, is the more firmly contracted. The motor nerves to the smooth muscles surrounding the proximal part of the urethra are the hypogastrics. Division of both hypogastric nerves in the cat, however, does not lead to paralysis of this part of the urethra, and consequent filling of it down to the compressor, although this lesion increases the intravesical pressure. After division of both pelvic nerves, division of the dorsal spinal roots of the sacral region on both sides, or after transection of the spinal cord, the proximal part of the urethra becomes distended down to the compressor urethræ [1]. Each of these lesions abolishes the first reflex, and therefore the intravesical pressure can rise much higher than normal, since micturition is no longer excited before this pressure has reached 10 cm. of water. The pressure necessary to force the urethra after paralysis of the compressor urethræ by division of both pudic nerves, therefore, when its resistance is entirely due to the smooth muscle surrounding the proximal part, is found to be rather more than 10 cm. of water. The explanation of the distended proximal urethra after these lesions is that the abolition of the first reflex allows the intravesical pressure to rise above that which is necessary to force the proximal urethra.

When animals are allowed to survive after nervous lesions, the observed effects are what would be expected from the facts which have just been described, and which were obtained by means of acute experiments.

Division of both hypogastric nerves in dogs was shown by Mosso and Pellacani [16] to be followed by no obvious effect on micturition. The dogs passed urine normally and showed that they knew when they wanted to. In cats the only effect is slight frequency of micturition [2].

Division of both pudic nerves in cats produces a varying degree of incontinence which is always slight. Sometimes it only amounts to the escape of a few drops of urine if the bladder is gently squeezed; at others a few drops of urine escape at times spontaneously, usually when the animal is making some straining movement, such as jumping.

The effects of the division of both pelvic nerves were first described by Lannegrace in dogs [14]; they are the same in cats. For the first few days there is retention of urine with overflow. During this stage the animals show no signs of discomfort, even if the bladder is squeezed through the abdominal wall. If pressure is maintained in this way, at first there is a very firm resistance to the escape of urine, but ultimately

the resistance suddenly gives way and allows the urine to escape from the urethra. The relaxation of the urethral resistance is so sudden and marked that it must be an active process. The period of retention with overflow is succeeded by one in which the animals are continent for long periods; they then pass urine in places deliberately selected by themselves, but the amount passed on each occasion is always small; they frequently pass small quantities in rapid succession. However often or however recently urine has been passed by these animals, there is always a considerable, and usually a large, volume of residual urine. This condition is permanent. If the hypogastric nerves are subsequently divided, the condition of the cat remains unaltered. If both pudic nerves are subsequently divided, however, the residual urine and the urethral resistance both become diminished, the retention with overflow becomes re-established and the cat ceases to show any signs that it knows when it wants to pass urine.

Division of the sacral dorsal roots in dogs [15], and in cats [1], produces retention of urine with overflow. The animals appear in no discomfort, they do not pass urine in jets and do not select places to pass it. When an attempt is made to express urine from the bladder, the urethral resistance is felt to remain firm and never gives the sudden relaxation felt after division of the pelvic nerves.

From the symptoms produced by these four lesions of the peripheral nerves, it follows that all the afferent impulses essential to micturition must enter the cord by the sacral dorsal roots through the pelvic and pudic nerves, that those which give rise to the pain of retention of urine must pass by the pelvic nerves, and that the pudic nerve carries afferent as well as efferent impulses leading to reflex opening of the urethra. It also follows that all the motor impulses essential to micturition must pass out by the sacral roots, but this does not exclude the possibility of inhibitor impulses passing out by the lumbar roots.

The effects of transection of the spinal cord on micturition are not obviously different, whether the transection is made between the origin of the two sets of nerves going to the bladder or in front of both. The immediate effect is retention of urine with overflow. After some days this gradually passes into automatic micturition. In this stage, which is permanent, urine is passed at intervals in a series of jets, the first usually being the largest. The jets often appear to occur spontaneously, but they can also be evoked by cutaneous stimuli in the perineal region or by anything calculated to increase the pressure in the proximal urethra, such as hypogastric pressure or holding the animal vertical [9].

The passage of urine is often associated with movement of the paralysed hind limbs. However much urine is passed there is always an appreciable residual volume. The force of the jets of urine is due to reflex relaxation of the urethra, and at the time it occurs the rhythm of the jets can be seen to be synchronous with rhythmic contractions of the superficial perineal muscles. The supervention of automatic micturition is associated with a progressive loss of tone of the compressor urethræ which follows the spinal transection. If urine is expressed from the bladder in the retention stage, the resistance of the urethra will be found to be very great, and to give way rhythmically, so that urine escapes in jets so long as pressure on the bladder is maintained. Each day after the transection the urethral resistance can be felt to be diminished, but the rhythmic relaxations remain. Spontaneous passage of urine in jets apparently takes place when the tone of the compressor urethræ is so diminished that the difference in the urethral resistance when the rhythmic reflex contractions occur has become significant in relation to the intravesical pressure. In the final stage of automatic micturition the volume of residual urine is considerably less than in the early stage of retention. No evidence of the first and second reflexes, which lead to strong bladder contraction, can be found in cats which have developed an automatic micturition after a spinal transection, and which have subsequently been decerebrated and examined in the way already described. There is therefore no reason to suppose that any recovery of reflex bladder contraction occurs with the appearance of automatic micturition after a spinal transection.

If a decerebrate cat is kept alive by carefully regulating the external temperature, spontaneous micturition can occur normally without any residual urine. The plane of decerebration passes approximately between the superior and inferior colliculi dorsally, and through the origins of the third nerves ventrally. It is clear, therefore, that all reflexes essential to the performance of micturition must arise behind this plane. The plane between the posterior part of the inferior colliculi dorsally and the middle of the pons ventrally has already been stated to contain the position of the first reflex. On exploration of this plane with a Clarke's instrument [12], it was found that there was a part of the brain, the destruction of which on both sides in cats was constantly followed by inability to empty the bladder, whereas the destruction of neighbouring parts was not. This part of the brain was situated a short distance ventral to the internal edge of the superior cerebellar peduncle, and extended from the level of the posterior end of the aqueduct in front to

the level of the middle of the motor nucleus of the fifth nerve behind. The smallest extent of the central nervous system, therefore, which is compatible with the performance of micturition must include this part of the brain in front and the origin of the sacral nerves behind, together with the connections between the two [3].

After destruction of either side of the posterior part of the aqueduct in its ventral half outwards to the mesencephalic root of the fifth nerve, micturition takes place normally, but the cat has no knowledge of when it is going to take place. This lesion, therefore, must have involved the centripetal path from the origin of the micturition reflexes to a higher part of the brain.

A urinary bladder is present in many fish. It is always situated on the dorsal side of the rectum, and its homology with the mammalian bladder appears, at least, doubtful. Nothing appears known about its nervous mechanism. In two eels, which had been anæsthetized with 1 per cent. ether water and the spinal cord divided just in front of the dorsal fin at the 21st and 22nd vertebræ, respectively, there was no abnormal dilatation of the bladder when they were killed with ether water after sixty-six and nineteen days respectively.

In other vertebrates which possess a urinary bladder, it is situated on the ventral side of the rectum, as in mammals. Except in eutherian and metatherian mammals, a cloaca is present into which the bladder and ureters each open separately.

A urinary bladder is present in all amphibians. In the frog its peripheral nerves were shown by Gaskell [8] and Horton-Smith [13] to closely resemble those in mammals. The 7th, 9th and 10th, but not the 8th, ventral spinal roots give rise to bladder contractions when stimulated, the 7th requiring a stronger stimulus than the other two. The fibres of the 7th pass to the bladder by the ramus communicans and the sympathetic, whereas the 9th and 10th fibres pass by the sciatic plexus. The spinal root arrangement was shown by Dale [6] to be the same in the toad. In the frog, toad, newt and spotted salamander [4] a transection of the brain between the cerebellum and mid-brain results in an over-distended bladder, whereas a transection appreciably in front of this level does not. The urinary bladder of amphibians, therefore, resembles that of mammals, not only in its rather complicated arrangement of peripheral nerves, but also in the fact that, although developed from the posterior end of the body and innervated from the most posterior of the roots of the spinal cord, it is controlled from the anterior part of the hind-brain. These facts point

to the conclusion that the bladder in amphibians and mammals is the same.

The only obvious use of a urinary bladder to a mammal is to prevent the animal smelling owing to saturation with its own urine. Otherwise the mammal would either fail to catch its prey or fail to escape detection, according to which of the two common modes of life it adopted. The bladder can hardly have been evolved for this reason, since urine only acquires an odour when the animal has developed the power of concentrating it, and the odour only acquires importance if mammals exist to smell it. It therefore appears that the mammalian bladder must have been evolved for a different purpose to that for which it is now used. The amphibian bladder cannot be of any use to the animal in the same way as the mammalian, since the urine is odourless. From its relatively enormous size it would seem that the amphibian's bladder must have some important function. It was believed by Townson [18] that a frog's bladder contained water, because the fluid in it was colourless and tasteless, and that though this water was frequently squirted to the outside when the animal was trying to escape, at other times the bladder served as a reservoir of water for the use of the animal when it was getting dried up. Subsequently it was found by Davy [7] that the fluid in the frog's bladder was urine, and Townson's hypothesis was neglected without any reason, since absorption of water from the urine occurs in the intestine of birds. If Townson's hypothesis is correct, the bladder was originally an organ for storing water and putting it into the circulation as required. In these circumstances the fact that the bladder acts from the anterior end of the hind-brain would become much less surprising.

Among reptiles a urinary bladder is present in the tuatara, in all chelonians and most lizards, and is absent in all crocodiles, all snakes and a few lizards; it is also absent in all birds.

In lizards the bladder is small and contains a very dilute solution of uric acid, yet white masses of solid uric acid are passed in the excreta, as in birds. It follows, either that some of the urine never gets into the bladder at all, or that the bladder periodically empties itself into the cloaca, the contents of which are not voided to the outside until water has been absorbed from the urine. In either case the bladder would seem to be in the process of degeneration. In four green lizards the cord was divided at various levels from the 12th to the 24th roots, and the animals kept alive from two days to ten weeks. In none was the bladder abnormally distended when they were killed. In another

experiment the cord was excised between the 26th and 30th roots, which includes the main part of the hind-limb plexus, the animal was killed in three weeks and there was no distension of the bladder.

The bladder is better developed in tortoises than in lizards. In the common land tortoise it not uncommonly contains soft concretions, but these are not common in the European pond tortoise. In seven European pond tortoises the cord was divided just behind the brachial plexus, and the animals kept alive for periods varying from two weeks to a year. In none of the seven was the bladder found to be distended more than it normally may be, and in two it was empty. A similar experiment was made on a common land tortoise which survived nine to ten weeks; in this case also the bladder was not distended. The same result was obtained in three European pond tortoises in which the cord had been divided at the 19th root, which is about the middle of the sciatic plexus, and the animals kept alive from one to fourteen weeks. In another European pond tortoise the cord was excised between the 15th and 23rd roots; when killed in three weeks the bladder contained only 12 c.c. It seems, therefore, that spinal transection is not followed by an over-distended bladder in reptiles.

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TRAUMATIC PNEUMOCEPHALUS.

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THE accidental entrance of gas into the cranial cavity, as distinguished from its formation there by organisms or its artificial introduction, has, in nearly all the reported cases, followed severe injury to the skull. The number of these cases is fifty, but the condition is certainly not so rare as this would suggest. The symptoms may be slight and the absorption of the air—the gas is always air in these cases—may proceed uneventfully, so that unless pneumocephalus is looked for it may pass unrecognized. On the other hand, a quarter of the recorded cases have ended in a fatal infection of the meninges. It seems, therefore, worth while discussing the origin and clinical features of this easily overlooked, but dangerous, condition, and reporting two more cases.

Case 1.—R W., a constable, aged 21, was admitted to the National Hospital, Queen Square, under the care of Dr. Gordon Holmes, February 28, 1927. In November, 1926, he was following some burglars on a motor cycle, when it skidded and he was thrown; his right hand and his legs were bruised and he felt dazed; he had not, however, struck his head. He gave up the chase and was returning when he collided head on with another policeman. They knocked their heads together, but the patient was not stunned, and was able with a little support to climb into a nearby lorry. He was taken to hospital, where he remained conscious until half an hour after admission; then he began to bleed from his left nostril. They packed his nose, and he was given morphia; then he lost consciousness. Next morning he awoke feeling fairly clear in the head, but his right eye began to show swelling and discoloration; his left eye also became "black," but was not as swollen as the right. He remained in bed in hospital for three and a half weeks. A skiagram showed a fracture through the nasal process of the right superior maxilla, as well as a fracture, with angulation, of the ethmoid. There was no evidence of air in the cranial cavity. On the first two days he had severe stabbing pains on the right side of his head, lasting for an hour or so. He vomited once. Eight or ten days after admission to the hospital a trickling of clear fluid had begun in his left nostril; this occurred especially when he bent his

head down. It lasted about a week and then stopped. He saw double in all directions for about three weeks after the accident; he still saw double when he looked downward. In January, 1927, he started work again, but gave it up within a week because his memory failed him.

In the middle of January he had an attack of influenza with headache, especially on the right side, coryza and cough and was confined to bed for three days. A day or two before, or a day or two after this, he was not sure which, his right hand suddenly "went stiff," by which he meant that a sensation like electricity went through his forearm and hand. The right hand became more awkward, and within a day or two he noticed that his right leg was becoming weak, and that he could not move the toes of his right foot. He could not comb his hair or hold a knife securely with his right hand, though it seemed strong enough. This condition of his hand improved, but he did not swing his right arm freely as he walked. The condition of his leg had not changed.

He was found to be a well-developed young man, pleasant, intelligent, and with apparently good memory. There was no disturbance of speech evident. Smell was much impaired; with neither nostril could he recognize any odours. The visual acuity of the right eye was $\frac{8}{20}$ with Snellen's types, of left eye $\frac{9}{20}$. There was no limitation of the visual fields. On ophthalmoscopic examination the right disc was found to have blurred edges and to show two dioptres of swelling; the left disc showed a little hyperæmia, but no swelling. Intraocular tension was 14 mm. in the right eye, 22 mm. in the left.

The pupils were dilated, the right larger than the left, circular and central. The left reacted well to light, directly and consensually, the right more sluggishly. Both reacted well on convergence. Movements of the eyeballs were good except on looking downward, when the right eye lagged behind the left and deviated a little outward, the patient then seeing double. The image seen with the right eye was about $\frac{1}{2}$ in. to the left of and underneath the image of the left eye, its lower part being slightly tilted to the right. Examination of the other cranial nerves did not show any disorder.

The other abnormal findings were awkwardness of the right hand, weakness and increased tone of the right lower extremity, slightly more active deep reflexes on the right side; variable, and at times a right-sided extensor plantar response, and a tendency to drag the right foot and to hold the right arm stiffly by his side when walking.

On March 1 the patient's head was X-rayed, and an area of diminished density was evident in the left fronto-parietal region.

By March 7 there had been improvement in the freedom of movement in the right lower limb and in the patient's gait; he no longer needed a cane, he dragged his foot less and held his right arm less stiffly. There was no change in the reflexes, but it was no longer possible to obtain any patellar clonus. Next day lumbar puncture was done; the fluid was clear and colourless, contained four cells per cubic millimetre and 0.03 per cent. total protein, and yielded negative Nonne-Apelt, Pandy, Lange and Wassermann reactions. His blood also gave a negative Wassermann reaction.

After the lumbar puncture he had headache when sitting upright and he thought his right hand became clumsy again. The headache disappeared gradually, however, and was never severe. His right hand and arm came to feel normal again, his leg improved and it was no longer possible to obtain an extensor plantar response. This state had been reached by March 21 and on April 14 he was discharged.

He was readmitted on June 1, 1927. For a fortnight after leaving hospital he had been well; then (April 29) while standing at the door of his home he suddenly felt ill and found that he could not speak plainly. He muttered, moved to a chair in which he sat down, and then became unconscious. Ten

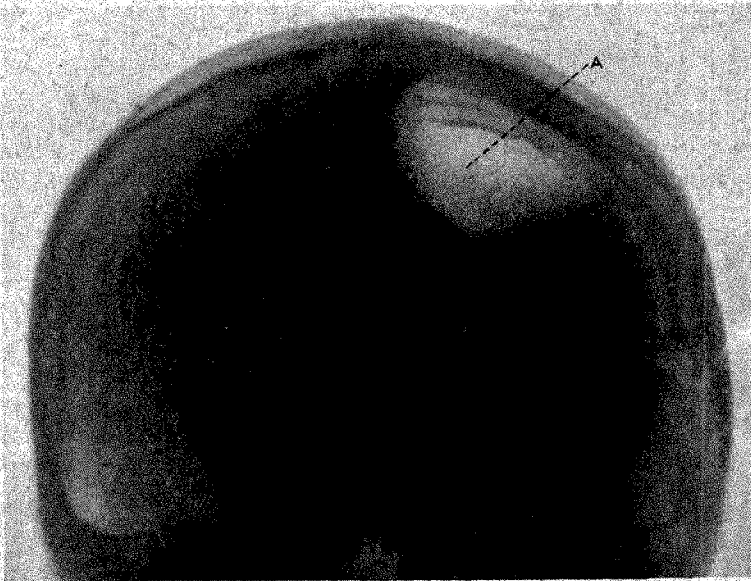


FIG. 1.—Antero-posterior view, showing subcortical collection of air (A) in left frontoparietal region. (Case 1.)

minutes later he recovered consciousness and after a few hours felt quite well and remained so for eleven days. He then had another attack, while out walking, in which he could not speak but remained conscious; he lay down and after a few minutes was able to continue his walk. He had felt well since then except for slight pain over the left side of his head a week before readmission. He still saw double when he looked down.

On re-examination his ability to recognize smells was found to have improved; his visual acuity was $\frac{6}{6}$ in each eye; both disc margins were indistinct, especially on the right side. The discs were very red and the veins full in the right retina. The size of the pupils and their reactions, the movements of the eye and the diplopia were as before. The examination of the motor system did not reveal anything abnormal; the reflexes were all

active and equal, except that the right plantar reflex was equivocal. It will be seen, therefore, that as far as physical examination went he had improved.

June 13 another radiogram was taken; it showed the same appearance as the previous one (see fig 1).

The patient was given a mixture containing sodium and potassium bromide, and during his stay in hospital (seventeen days) he remained well.

He went home and remained well for six days; then (June 24) while reading, he suddenly found that he could not speak plainly but could only make burbling noises; he remained conscious and after he had lain down for a minute it was all over and he could speak easily. He did not have any headache after it. The next attack was on July 23; he suddenly found himself unable to speak articulately, stepped inside a room and lay down and the last thing he remembers was that his head and neck curved back to the right. He was unconscious for a quarter of an hour, coming to himself gradually. The only subsequent attacks had been on September 23; one occurred during the night, and half an hour after waking up on the following morning he had another attack during which he did not become unconscious. After this fit he could not speak plainly for ten minutes. "I could think plainly but I could not utter my thoughts in words."

For a day and a half before the attack in July he had a numbness in his right leg which was no longer present after the attack, but he had had this numbness since to a less degree, lasting about half a day and not followed by an attack.

He was found when he was readmitted to hospital on September 27, 1927, to be in good general health, quick, co-operative, pleasant, with good memory and grasp; occasionally he hesitated for a word and once or twice he stammered. He could not distinguish odours, but was aware of very strong ones, such as asafoetida. Visual acuity was $\frac{6}{6}$ with each eye. The visual fields were of normal extent. The edge of the right optic disc was a little blurred and the disc slightly swollen (0.5 dioptries), the left disc was normal. The pupillary reactions and diplopia were as at previous examinations. Apart from these findings nothing abnormal was discovered; both plantar reflexes were flexor.

He had constant slight headache over the left side of the top of his head and he complained of numbness in his right leg.

By October 18, the indistinctness of the edges of the right disc had become more evident and it was pinker; there was also some blurring of the temporal edges of the left disc.

October 29, another radiogram was taken; the same large, sharply defined translucent area was to be seen in the left parietal region over the upper part of the Rolandic area. It was, however, slightly smaller than before.

There was not any tenderness anywhere over the skull and there was no difference observed in the percussion note.

On October 28, 1927, an operation was performed by Sir Percy Sargent. A large flap of bone was turned down over the left parietal region and on opening the dura mater, which was not noticeably under tension, an area of brain

limited at the midline, and laterally, in front and behind by the markings of the veins and sulci, was seen to be bulging slightly. It was much paler than the surrounding regions. Its posterior border was $\frac{1}{4}$ in. anterior to the Rolandic fissure; it measured 2 in. antero-posteriorly, $1\frac{1}{2}$ in. to $1\frac{3}{4}$ in. from side to side. Several veins coursed over it and the markings of the smaller sulci were visible. A hollow needle was inserted and the surface of the pale area sank in quickly. When the opening was enlarged yellowish fluid and a few bubbles of gas escaped. The cavity was fairly large, it was situated in the substance of the brain, had smooth walls which were a little darker than ordinary brain tissue; washings from the first irrigation of the cyst were saved and examined but no spectroscopic or other evidence of changed blood was found. After irrigation the dura mater and the bone flap were replaced and the skin edges apposed.

On the morning of the day after operation he seemed fairly well and cheerful and spoke plainly. He had headache. Early in the next morning he had a fit which lasted seven minutes and was followed by aphasia and paralysis of all movements of his right wrist and fingers; he held his fingers flexed. No abnormal signs were found on the left side. On the right side neither supinator, biceps or triceps reflexes could be elicited; a quick upward movement of the great toe followed plantar stimulation.

Within two days the aphasia and other symptoms cleared up.

By November 16 he felt well, had no headache, but the papilloedema was still considerable. During the rest of his stay in hospital he was well, his wound healed and the diplopia was the only abnormal physical sign, save for the slight papilloedema which persisted. Another radiogram was taken November 30, 1927, which showed no trace of gas remaining.

Early in February, 1928, he had another fit. On March 14 he came to the hospital; re-examination of the eye-grounds, the reflexes, the motor and sensory systems showed nothing abnormal. Five days after this he had another fit, and during the following fortnight two more. The fits were of the same kind as those described above; during them he has bitten his tongue and passed his urine. He also, for two or three days at a time, had feelings of numbness in the right side of his body.

Case 2.—A. S., aged 46, was thrown from his bicycle on September 16, 1927, injuring his right shoulder and the right side of his head. There was bleeding from his nose which continued for two hours. About an hour and a half after the accident he became gradually unconscious and vomited altered blood; his eyelids were swollen with extravasated blood, so that his eyes were completely closed. There was a depression about the size of a halfpenny on the right side of the skull. He recovered consciousness after twelve hours, and improved so that ten days later he got up. It was then noticed that there was a watery discharge from his nose, and this had continued ever since. During the third week after the accident he became incontinent, drowsy and began to vomit. On October 22 his skull was trephined and blood-clots removed from the temporo-sphenoidal region. He seemed better after this, but

was still occasionally incontinent; he gradually became drowsy and would not eat because swallowing made him cough, and this increased his headache; the headache was in the forehead and behind the eyes. During December he became stuporose, and on January 4 he was admitted to the National Hospital, Queen Square, under the care of Dr. Gordon Holmes.

He was found to be stuporose; his temperature was 101.8°F. , the pulse rate 140. So far as it was possible to examine the cranial nerves, nothing abnormal was found. The deep reflexes were more active in the left side of the body

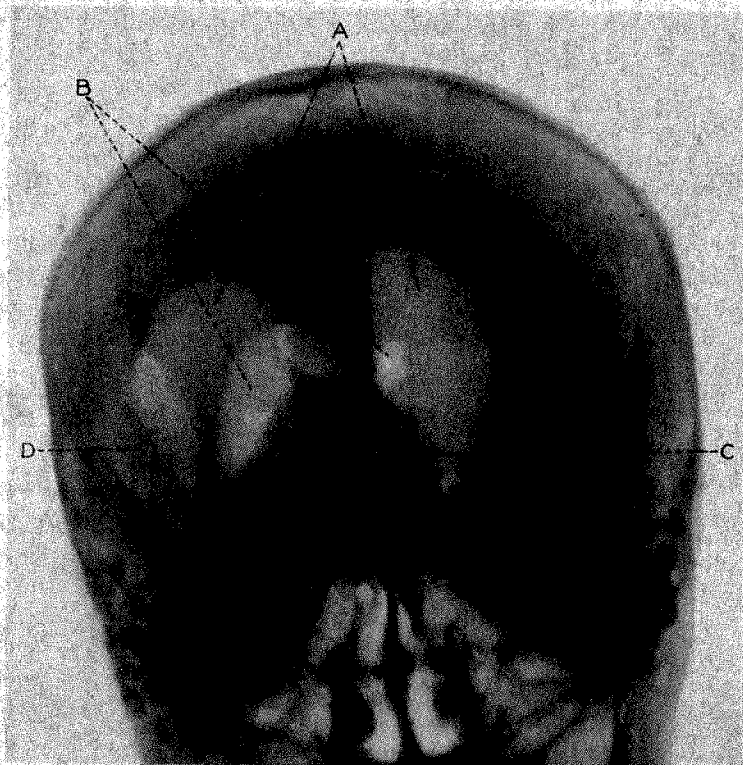


FIG. 2.—Antero-posterior view, slightly oblique, showing air in the frontal lobes (A), in the lateral ventricles (B), and in the third ventricle (C). The trephine wound can be seen on the right side (D). (Case 2.)

where there was also an extensor plantar reflex. The left hand was tremulous and wrist-clonus could be obtained. He was incontinent of urine and faeces. His back and neck were rigid, and Kernig's sign was present on the left side. There were bedsores on both lower extremities. Over the right side of the forehead was a scar (from the operation) and a defect of the bone as large as a hen's egg. The cerebrospinal fluid was colourless, but turbid, with a flocculent coagulum. There were 950 cells per cmm., of which 70 per cent. were poly-

morphonuclear, 30 per cent. mononuclear. The chloride content was 0.75 per cent. There was rather weak direct reduction of Fehling's solution. No organisms were seen in films.

A radiogram was taken on January 5, 1928; besides the trephine wound in the right side of the skull, the appearances of gas could be seen in both frontal lobes, the collections communicating with each other, in the lateral and third ventricles and the basal subarachnoid space (see figs. 2 and 3).

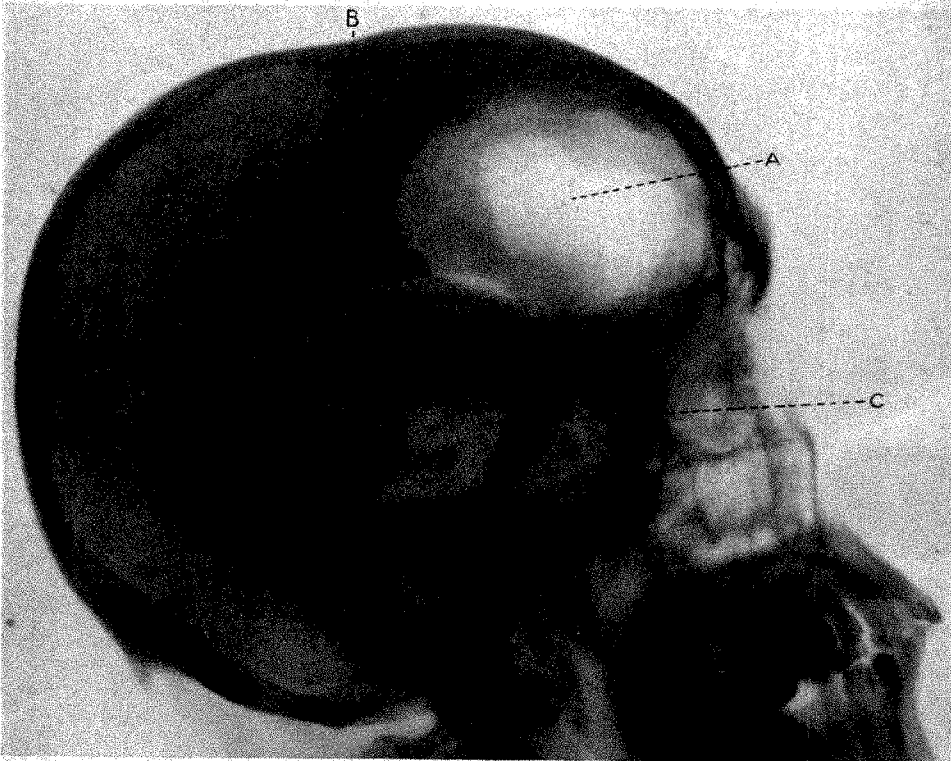


FIG. 3.—Lateral view showing air in the frontal lobes (A), in the lateral ventricle (B), and in the basal subarachnoid space (C). (Case 2.)

The patient remained stuporose, taking only fluids and coughing a good deal, until his death on January 7. During his stay in hospital no rhinorrhœa was observed.

At autopsy (Dr. J. G. Greenfield) a trephine wound was found in the right fronto-temporal region. The convolutions were flattened at the vertex, and there were yellowish purulent streaks besides the veins in the vertical sulci; over the cerebellum was reddish sanio-purulent exudate. The right frontal lobe was slightly adherent to the dura, and was soft and boggy. The left lobe was similar but thinner-walled, and on removal burst, leaving a part of

its wall attached to the cribriform plate of the ethmoid and the overlying dura mater. In each frontal lobe a cavity was seen, communicating by a channel about 1 cm. in diameter with the anterior horn of the lateral ventricle of the same side. The cavity on the left side was for the greater part smooth-walled, that on the right side had a somewhat roughened wall from infection, and it contained sanio-purulent fluid like that in the posterior fossa. There were numerous small vessels to be seen on the walls of the cysts. The general shape and situation of the cavities may be seen in the accompanying photo-



FIG. 4.—Horizontal section, showing the frontal cysts, each communicating with the lateral ventricle of the same side. (Case 2.)

graph of the brain in horizontal section (fig. 4); the depth of the right cavity was 5.6 cm., that of the left 4 cm.

On removal of the brain-detritus from the left cribriform plate a hole was found through the dura and bone about 1 cm. behind the crista galli, through which a probe could be passed into the left nasal space. Owing to the tearing of the brain tissue it was not possible to determine whether this opening still communicated with the cyst on the left side. No injury of the right ethmoid plate was observed. The orbital surface of the right frontal

lobe was bruised. There was no infection of the sphenoidal or ethmoid sinuses. In the visceral organs bronchopneumonia and early atheroma at the origin of the aorta were found.

Microscopically: sections of a smooth part of the cyst wall showed proliferation of neuroglial tissue with swelling of neuroglial cells and a little round-celled infiltration around the vessels, with many plasma cells.

GENERAL CONSIDERATIONS.

The first of the above cases is a typical one. No matter what the cause of the opening in the skull—a gunshot wound, a “head-on” motor collision, a fall, an eroding pituitary tumour, an intracerebral abscess, an operation—the general features of the condition are uniform; a lesion opening the inner wall of one of the cranial air cavities (most frequently a fracture into the frontal or ethmoidal cells), an escape of fluid from the neighbourhood of the fractured bone, symptoms of an irritative or space-limiting intracranial lesion, and an X-ray picture by which one can recognize that there is gas in the cranial cavity. These features are present in the cases recorded above. It must be admitted, however, that none of these is always present. Thus, in Wodarcz’s case the cranial air sinuses were intact, the entry of air occurring through a peculiar valvular opening in the parietal wall (cf. also Scott and Hansemann). In a number of cases no escape of fluid from the nose or ear was observed. The condition has been discovered by accident in patients who seemed quite well; in Chiari’s and Wodarcz’s cases no radiogram was taken, while many cases have been diagnosed because of the history and symptoms, independently of an X-ray picture, or else the latter has been overlooked and the condition first recognized at operation or autopsy. Where adequate skiagrams have been taken they are decisive in settling the diagnosis.

The mere discovery of the presence of air, however, is not of great moment from the point of view of treatment or prognosis; in order to get light on these matters one must consider how the air has entered the cranial cavity, where it has lodged and what has happened to the track along which it passed.

There are diverse statements on these points, corresponding no doubt to the varying features of the individual cases. The following are some of them. Air enters the subarachnoid space at the time of injury, or within a few hours, and passes by the foramina of Luschka and Magendie into the ventricular system. Air gets into the ventricles directly through a tear in the wall of the third ventricle. Lacerated

brain tissue undergoes colliquative necrosis and is replaced by fluid which flows away through the cranial aperture and is in its turn replaced by air. Air enters the subdural space and remains there for weeks or months. Sneezing, coughing, straining or nose-blowing drives air into the damaged brain directly from without, or a subdural accumulation of air during such tension-raising exercises breaks through into the lateral ventricle or forms an air cyst in the cerebral substance. A valve is present which lets air in but not out; it lets fluid out, however. The air enters from the frontal, ethmoid or sphenoid sinuses or from the mastoid. A fragment of shell draws air into the skull behind it or forces it in ahead; a shot in the mouth raises the pressure in the upper air spaces to such an extent that "coincidentally with the shot a certain quantity of air or other gas penetrates into the interior of the skull," or even, somewhat transcendently, "as a result of the sudden application of force to the skull there is in some way produced a certain degree of negative pressure within the calvarium, and into this vacuum there is aspirated ahead of the expanding brain a certain amount of air."

Though some of these statements are disputable it is sufficiently plain that the development of pneumocephalus does not always come about in the same way. Hence rules for operative treatment have been laid down which might have been more properly restricted to cases like those the writer had observed. The different conditions which favour the entry of air into the skull and the effects it produces are, therefore, of considerable importance.

One of the main requirements for the development of the condition is a tear of the dura mater; only one case of epidural aerocele has been recorded (Reisinger) and many later writers have doubted the accuracy of this diagnosis. The paramount rôle of the dura mater in keeping the cranial cavity closed is shown in the cases of "spontaneous" cerebrospinal rhinorrhœa, in which rupture of the dura has been followed by a leakage into the nose of cerebrospinal fluid (Locke [12], Matzdorff [14]). Since it is in fractures of the base of the skull and of the frontal bone that the air sinuses are laid open, the close attachment of the dura to the bone in these regions is a favouring factor.

Upon the point of entry of the air chiefly depends its immediate site of lodgment—whether subdural, or subarachnoid and ventricular. Dandy has pointed out that whereas in the neighbourhood of the posterior ethmoidal and sphenoidal cells the subarachnoid space with its cisterns is capacious and the subdural space scarcely existent, it is quite otherwise as one approaches the convexity of the brain; so that

where air enters the skull through the frontal or anterior ethmoidal cells it must pass into the potentially large subdural space, for there is no room for it here beneath the arachnoid membrane. Bullock's statement that a subdural collection of air, "external pneumocephalus," is always the primary stage in the formation of intraventricular or intracerebral pneumatocele therefore needs to be qualified unless one assumes from his silence about subarachnoid collections that any form of extracerebral air is included in the term "external pneumocephalus," which he uses as a synonym for subdural pneumatocele. These considerations have an important bearing on the appearance of the most characteristic symptom of the condition, a flow of watery fluid from the nose or ear. It is evident that where there is a true liquorrhœa, i.e., where it is cerebrospinal fluid that escapes, either the subarachnoid space or the ventricles have been opened. The escape of large quantities of cerebrospinal fluid could scarcely occur from the subarachnoid space of the frontal region; there might be a considerable subdural pneumatocele here without any liquorrhœa being observed, and on the other hand the copious escape of fluid after a frontal fracture will point strongly to a transcerebral irruption of air into the lateral ventricle (cf. Eggers' case).

The immediate location of the air is of prognostic importance; in the subdural space air may remain unabsorbed for over ten months (Cotte's case), whereas from the subarachnoid space in small quantities its absorption is a matter of hours; since, however, subarachnoid air is usually associated with filling of the ventricles also, the complete absorption may take about a fortnight, supposing the influx has ceased, although the bulk of the air disappears in three or four days. The findings after the artificial introduction of air for diagnostic purposes, pneumoventriculography, tally with those obtained in these cases (cf. Jacobi [11]).

There is the further prognostic consideration that infection is more likely to reach the meninges in the presence of sphenoidal and posterior ethmoidal lesions which open up the basal cisterns. Teachenor [19], however, bases his advocacy of draining the frontal sinus after compound fracture on the great likelihood of infective material being forced into the cranial cavity and leading to meningitis. The path of infection in the fatal cases of pneumocephalus after frontal injury is difficult to determine, as drastic operative measures had been undertaken, including removal of part of the wall of the sinus. The almost inevitable death from meningitis of patients with "spontaneous" cerebrospinal rhinorrhœa,

in which the lesion is usually in connection with the basal subarachnoid space, is evidence of the greater danger of openings into the latter.

To speak of the escape of fluid as cerebrospinal rhinorrhœa or liquorrhœa is not always right. The fluid may be a reaction-product. Where there is a copious flow one would conclude that it is cerebrospinal fluid that is running away, and in some cases tests have shown that this is so, but since air is a mild cerebral irritant and may lead to the production of a sero-sanguinous fluid there are, no doubt, cases where from the air-filled defect in the injured brain fluid drains away that is a mixture of broken-down brain-tissue and exudate, due partly to the irritation of the air and partly to the trauma. That the irritative effect of air alone is not necessarily great may be seen in Santoro's case where air was present in the ventricles for over a year without any symptoms except rhinorrhœa.

It has often been taken for granted that the air has been forced into the skull during sneezing, coughing or straining, and has been trapped there, as it were, and so led to increase of intracranial tension and this in turn to liquorrhœa; others of a contrary way of thinking have pointed out that there is nothing to stop cerebrospinal fluid running away once the subarachnoid space or the ventricle is in communication with the outside air, which then, of course, enters to replace the fluid. As for the latter explanation, it plainly does not suffice for all cases since considerable collections of air have been found though there had not been any precedent liquorrhœa; that it is, however, possible for the entry of air to be secondary to the escape of fluid is seen in Santoro's unique case where a patient with, in all probability, a pituitary tumour developed copious liquorrhœa which lasted for over a year; in a radiogram the very distended ventricles, including the third, and the basal cisterns were seen full of air and there can be no doubt that the escape of fluid preceded the entry of air, as the author supposes, though he postulates two openings, one into the sphenoidal cells through which fluid escaped and air entered directly into the third ventricle, and another "collateral aperture due to the process of erosion" through which air infiltrated the subarachnoid space. It might, however, be objected that in this case there was increased intracranial tension prior to the escape of fluid, whereas, of course, normally the intracranial tension is lower than that of the atmosphere, so that there is no reason why cerebrospinal fluid should flow away. But in the normal person the effect of coughing and straining¹ on the pressure of the cerebro-

¹ How this rise of pressure comes about is uncertain. Thus Tzanck and Renault [20],

disappeared by the end of the week). This is by no means always so, as a number of instances, with series of plates, attest. After the initial injury with its usually slight escape of cerebrospinal fluid, the hole in the dura is probably sealed with coagulum until force from within or without bursts it open again. One may compare Adolf Meyer's case of rhinorrhœa, in which the flow ceased for a while when the patient had a cold; he then went into a deep sleep which passed off when the flow was re-established. A good deal of weight has been laid on whether the rhinorrhœa is intermittent or continuous, but since the passage of small quantities of fluid could scarcely be distinguished from ordinary nasal secretion, and the trickling of fluid into the pharynx may pass unnoticed, it is very hard to say whether an apparently intermittent flow may not be a continuous one of varying quantity.

Similarly the increase in the flow when the patient bends his head forward may be ascribed not only to the pressure changes already mentioned, but also to the diversion of fluid from the pharynx into the nose. It has been recorded in many cases of "spontaneous" rhinorrhœa, and to regard it when pronounced as definite evidence of a cystic collection of fluid which runs over (see Dandy's article) is too sweeping. Definitely intermittent discharge is almost always associated with symptoms of increased intracranial tension, which it relieves; it tends to persist for a long while. The cessation of rhinorrhœa is a valuable indication that the entry of air has probably stopped and the opening become occluded. In Passow's case, seven weeks after air had entered the skull the profuse rhinorrhœa came to an end; four months later the patient got severe headache, and there was a further copious flow from the nose (cf. Sir James Paget's case of rhinorrhœa [15] in which the interval of freedom was a fortnight, and Elliotson's case [6] where the liquorrhœa beginning when the patient was 26, and ending thirteen months later, recurred when the patient was 40, and kept on for two years).

Air in the cranial cavity may lodge (1) in the subdural space; (2) in the subarachnoid space; (3) in the substance of the brain; or (4) in the ventricles.¹

¹ As to terminology: "Pneumocephalus" or "pneumatocephalus" is the general term applied to every variety of the condition, Bullock suggesting the division into internal and external, just as in hydrocephalus. "Pneumatocele" or "aerocele" covers all but the intraventricular variety. "Pneumocranium" is also used occasionally. "Cerebral pneumocyst" is a term suggested by Verebely, and adopted by Siegmund in his article dealing with these cases. "Pneumoventricle" and "pneumencephalon" are also used, but

There has been much discussion in the literature about the path of ventricular air—whether it enters from the subarachnoid space through the foramina of Luschka and Magendie, or passes immediately through a tear in the third ventricle; the point is evidently one to be settled at autopsy, if at all. More significant are those cases in which air has passed through the substance of the brain from the subdural space into the ventricles, such as must be the sequence where the lesion is of the frontal sinus (Lockett, Wolff, Dandy's first case), or where only one lateral ventricle is filled with air (Colle, Eggers, though the latter writer supposes it otherwise. It is necessary to assume a blocking of the foramen of Monro in these cases). During sneezing, &c., the air is forced into the necrotic injured brain substance, and either digs out a hole for itself, so forming a cerebral pneumocyst, generally with fluid in it as well, or it penetrates to the ventricle and causes pneumoventricle alone, or a cyst communicating with the ventricle. Later, the air in the ventricle may be absorbed and the ingress of more air precluded by the falling together of the brain tissue, clotting and scarring, so that an intracerebral pneumocyst remains in which the air is under tension (cf. Blau's case); in many instances it is recorded that the overlying convolutions were flattened and bloodless. In rare instances it is possible for the air to be absorbed from such a cyst, only fluid remaining (Glénard and Aimard, with autopsy findings by Barbé and Glénard; Horrax, Goldammer).

The entry of air into the brain is generally supposed to occur when the cerebral substance has softened sufficiently to permit it, but this softening is a rapid process, requiring only a few days, and the late development of the lesion may be with more probability referred to the general conditions determining air entry into the skull. In many cases adhesions of the dura to the bony opening have been found; in such it is of course unnecessary to suppose any intermediate subdural accumulation of the air that is driven into the brain substance. When air that has been in the subdural space or in the cerebral white matter bursts into the ventricle, there may be not only sudden alleviation of the symptoms, but also complete absorption of the air (cf. Potter's case). The commonest of these symptoms is headache; it is, however, important to remember that headache may be evidence of diminished

the latter is so identified with the diagnostic procedure introduced by Dandy, that its use in connection with the traumatic air collections is inadvisable.

"Pneumatocele of the cranium" has, unfortunately, also been used to designate subperiosteal collections of air, following lesions of the frontal or the mastoid sinus (cf. McArthur [21]).

as well as of raised tension, and diminished cerebrospinal pressure, as measured in the lumbar region, has been reported in at least two cases of pneumoventricle (Schloffer, Santoro).

It may seem strange that the air should travel so far as from the cribriform plate to the pre-Rolandic area, immediately beneath the cortex; but the area of damaged brain, after cranial trauma, corresponds roughly to "a projection of the line of action of the force applied"; for example, a man fell on the side of his head; six days later he died, and it was found that between the site of injury and a "contrecoup" point in the occipital region, over which the soft parts were suffused with extravasated blood, there stretched a continuous band, evident to the naked eye, of swollen and degenerated white matter (Hauser [10]). Thus in fractures of the posterior part of the skull the air cysts have been found in the occipital lobe.

Some intracerebral cysts reach the surface and have as their outermost boundary the dura mater (Passow), the bone, or even the skin (Manasse). In Passow's case the cyst was surrounded by a delicate vascular wall, which he ascribed to the reaction of the brain tissue. Where, however, the cyst is entirely intermeningeal, it is hard to say why it should be localized, as most subdural aerocèles are; adhesions consequent on traumatic meningitis or irritation may be partly responsible. There are, indeed, a number of difficult points in connection with the development and course of this condition, discussion of which would be mostly "wide conjecture."

COURSE OF EVENTS IN THESE CASES.

Case 1.—Since no radiogram was taken during the rhinorrhœa, and since the patient happily did not reach the autopsy room, one cannot be quite certain as to what happened. It seems most likely that at the time of the rhinorrhœa air entered the skull by way of the fracture in the fronto-ethmoid region, settled under the dura and in the damaged and colligated substance of the brain, and probably also burst into the left lateral ventricle, so occasioning the escape of fluid from the nose. Once the air had reached the vascular system it was absorbed fast enough to obviate any considerable rise of pressure, so that the dural opening could be sealed, the liquor œa came to an end, and the opening into the ventricle closed also. The patient's state then remained unchanged until he caught a cold; during paroxysms of coughing the intracranial pressure was raised, the volume of the brain momentarily increased, and the air that had remained unabsorbed in the subdural

space was forced along the old track, now become a blind alley, into the cyst-like end, where the sudden irritation and displacement of surrounding tissues led to such symptoms as awkwardness, and "peculiar sensations" in the right upper extremity and weakness in the right leg coming on suddenly, progressing for two days, and then remaining about the same. The gap in the brain substance was then mostly filled by granulation tissue; there was left a subcortical cyst containing air and a little fluid, which did not alter perceptibly during many months.

In support of this are the following considerations. The situation of the bony lesion was not such as would lead to opening of the large basal subarachnoid collections, so that the rhinorrhœa could hardly be accounted for in this way; the damaged parts of the brain would be already softened a week after the accident, so that the entry of air into the cerebral substance would be almost inevitable once it had penetrated the dura mater. Rhinorrhœa in this case must indicate either the production of an irritative fluid or rupture into the ventricle, and the absence of focal symptoms is in favour of the latter; cessation of rhinorrhœa suggests either that the cranial opening has closed, or that the source of fluid has become shut off from the exterior, and as the latter is not likely to happen as long as air is entering, it is evident that the cranial, i.e., essentially the dural, opening must have closed; moreover, later on the patient got coryza, and yet infection did not spread to the brain or its membranes; the intracranial forces driving air inwards and leading to the focal subcortical symptoms were not sufficient to reopen the dura or the ventricle.

Case 2.—Through the opening in the cribriform plate of the ethmoid, air was able to penetrate into the left frontal lobe, and so directly into the ventricles, leading to a continuous escape of cerebrospinal fluid; either then, or later owing to trauma when the skull was trephined on the right side, air was forced into the right frontal lobe also. Infection occurred through the still patent opening, and by the swelling and exudate so caused the outflow of cerebrospinal fluid was obstructed. The occurrence of air-cysts in both frontal lobes is unusual, and in this case the development of that in the right frontal lobe was probably related to operative trauma.

The appearance of the cyst wall on section may be contrasted with that of Barbé and Glénard's case in which the cyst, filled by replacing fluid, had an ependymal-like lining wall with a deeper layer of sclerosis.

SYMPTOMS AND DIAGNOSIS.

There may be no symptoms at all or only mild headache; or there may be severe headache, dizziness, vomiting, slow pulse, convulsions, hemiplegia, stupor or psychic changes of the Korsakow type; papilloedema has been occasionally found. Liquorrhœa is a very important sign. Pathognomonic, but infrequent, are a tympanitic percussion note over certain parts of the skull and a characteristic succussion sound (Plätschergeräusch) heard by the physician and sometimes also by the patient when he shakes his head. This has been observed also in cases reported by Bonhoeffer [2] and by Mühlmann, where air was aspirated through a needle used for puncturing a hydrocephalic distended ventricle. It may be the most prominent symptom, and has been described as "just like shaking a coconut" (Scott, Mothersole). The hissing noise as the air passed through the valvular opening in Wodarcz's case may be looked on as a clinical curiosity. In Colle's case there was gaseous crepitation of the tissues in the frontal region near the wound. Other symptoms due to the original trauma may, of course, also be present. Evidently the common symptoms, apart from liquorrhœa, are those of a tumour (or of sudden, perhaps transient, hydrocephalus) and are not particularly characteristic.

For diagnosis a radiogram is, of course, indispensable. The appearances do not always permit of accurate localization, and concerning many of the reported cases, in which the X-ray pictures are available, one finds subsequent writers disputing the original conclusions on this point. Stereoscopic pictures usually leave no room for doubt. Even after operation, however, it has occasionally been uncertain where the air really was (Reisinger's case might almost be called notorious in this respect). Occasionally the X-ray indications are overlooked, e.g., Brünig. In cerebral pneumocysts there may be a horizontal inferior border (Flüssigkeitspiegel) due to the fluid present and readily recognizable on screening (cf. Duken). Where the air is in the ventricles and the subarachnoid space, the picture is the same as that obtained in artificial pneumoventriculography. By this diagnostic method, which has been applied to all sorts of disorders of the central nervous system, the Breslau neurologists especially (Foerster [9], Schwab [17]) claim that one can discover late traumatic changes in the brain and its membranes not otherwise to be detected during life; the validity of their conclusions has been questioned (Bonhoeffer [3], Jacobi [11]), but their views are mentioned here because some cases are on record in which from the history and findings it appears possible that an

unsuspected traumatic pneumocephalus may have been present before air was pumped in on purpose by the neurologist. Foerster's remarkable Case 41 [9] (Case 7 of Schwab) and Locke's third case [12], may be mentioned as having occasioned such doubts, in the absence of any report on the X-ray findings prior to pneumocephalography.

In general, whenever a patient who has had rhinorrhœa after cranial injury complains of symptoms such as headache, the possibility of air collection must be borne in mind, even if there has not been any copious discharge, but merely trickling just after the accident (cf. Wheeler, Monari), or even if earlier radiograms did not point to aerocele.

PROGNOSIS AND TREATMENT.

Nearly all the deaths have followed operation—operation generally undertaken, to be sure, because of the severe symptoms of raised tension or of meningitis; the cause of death has been meningitis. Infection is especially liable to happen when the basal cisterns have been opened; a rise of intracranial pressure, militating against the gradual occlusion of the cranial opening, adds to the risk. The danger to life, then, lies in meningitis; operation possibly increases the risk, but there are insufficient data for any conclusion on this point—certainly some cases get well after operation and a good many do perfectly well without it. Apart from this, prognosis is chiefly concerned with the length of time before the air can be absorbed, and the likelihood of the lesion causing permanent symptoms such as fits. As to absorption, its duration will depend on the situation of the air and the closure of the way in; once the air can no longer get into the skull, if what is already there is in the ventricles and subarachnoid space, it will be absorbed entirely in one or two weeks; in the subdural space it may remain for ten months or longer (Cotte) or be absorbed in a month (Nessa); in the substance of the brain it usually persists unchanged for an indefinite period, as in the first of the cases here recorded; in others it has been absorbed, and one cannot tell on what these differences depend. Symptoms referable to the lesion after the air has been absorbed have not been observed in the small number of case-records bearing on this point.

Prophylactic measures have been advised; surgical repair of the bone and dura immediately after a compound fracture of the skull will come under this head, but the other precautions recommended must be inadequate if they are not absurd: one cannot stop a man from sneezing and swallowing.

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CHANGES IN INTRACRANIAL PRESSURE DURING FORCED DRAINAGE OF THE CENTRAL NERVOUS SYSTEM: THE HYDRATION FACTOR.¹

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By "forced drainage" is meant the administration of water by mouth, or the intravenous or subcutaneous injection of hypotonic saline solution, at the same time allowing the free escape of the cerebro-spinal fluid. A series of recent studies led to the conclusion that by this procedure it is possible to accelerate markedly the formation of cerebro-spinal fluid [3]. Furthermore, it was observed that the application of this process of "forced drainage" to an animal suffering from encephalomyelitis caused a remarkable extrusion of the perivascular cellular exudates from the depths of the tissue into the subarachnoid space. Such a phenomenon is illustrated in figs. 1 and 2, which are taken from the spinal cord of a cat which had been subjected to a prolonged trypan-blue meningitis, with forced drainage instituted just before death. In fig. 2 a plug of lymphocytes is seen in the perivascular tissue in the depths of the cord, while in fig. 1 the lymphocytes lie in a heap over the opening of the perivascular channel into the subarachnoid space. In the higher magnification of fig. 3, a zone of phagocytes filled with trypan-blue can be seen along the outer border of the mound of lymphocytes. (Taken from the study of Kubie and Shults [3]).

The possibility of instituting in this way a physiological lavage of the central nervous system, with a partial washing-out of inflammatory products from the depths of the tissues to their surfaces, arouses a hope of therapeutic application. It is with serious misgivings, however, that one faces the possibility that the procedure of forced drainage might result in a dangerous increase of intracranial pressure. The aim of this communication is to indicate that during forced drainage an entirely negligible rise in intracranial pressure and no demonstrable

¹ Presented before the meeting of the Association for Research in Nervous and Mental Disease, December 28, 1927, New York City, N.Y.

hydration of the tissues of the central nervous system occur. The results of previous studies of the question will be presented briefly; and the investigations which have just been completed will be described in greater detail.

The problem was first studied on a group of normal, anaesthetized dogs [1]. Fig. 4 (from the report of this study) shows the method used for measuring intracranial pressure while allowing a free flow of cerebro-spinal fluid from a needle in the cisterna magna. As a result of this study, it was concluded that during forced drainage the intra-

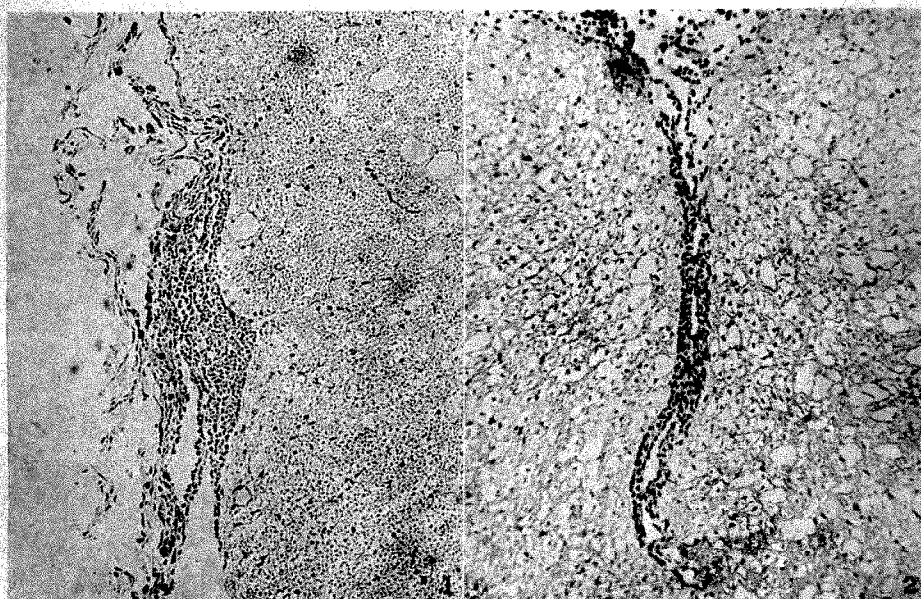


FIG. 1.—KC12x. Lymphocytic infiltration in the perivascular tissues of a cat suffering from a trypan-blue meningo-encephalitis. A short, forced drainage, instituted just before death, had been prematurely terminated by an overdose of anaesthetic. $\times 200$.

FIG. 2. - KC12x. Lymphocytic infiltration extruded from the perivascular channel of the same animal as in fig. 1, and lying in the subarachnoid space. $\times 200$.

cranial pressure (which had dropped nearly to zero during the preliminary drainage) never rose above, and only rarely reached, the initial normal level.

The second study of the question was undertaken during the past summer, in the Massachusetts General Hospital and the Children's and Infants' Hospitals of Boston, through the kindness of Dr. James B. Ayer, Dr. Bronson Crothers, and Dr. Kenneth Blackfan. The full report of the work will appear in an early number of the *Archives of*

Neurology and Psychiatry [2]. Examinations were made of patients who were suffering from many forms of infection of the central nervous system; and on them, obviously, no direct measurements of intracranial pressure could be made if the cerebro-spinal fluid was to be

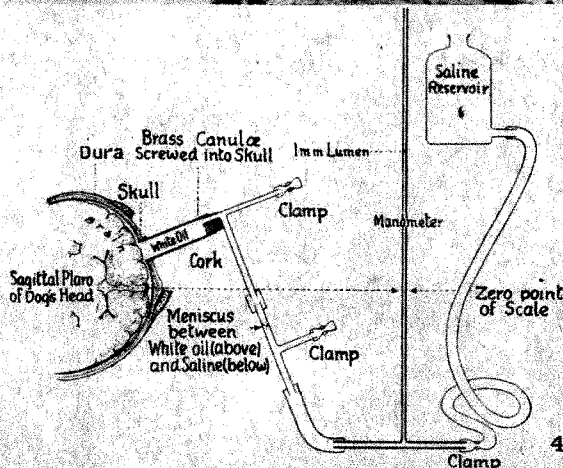
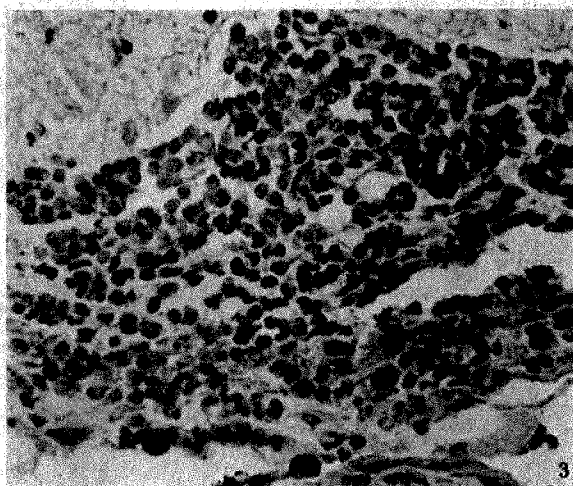


FIG. 3.—KC12x. Same as fig. 2, at 700 magnification. The contrast between the macrophages of the outer zone, filled with ingested trypan-blue, and the deeper zone of lymphocytes is just visible in the photograph.

FIG. 4.—Method of measuring intracranial pressure with free drainage of the cerebro-spinal fluid (see text from Kubie [1]).

allowed to escape freely from a needle in the lumbar subarachnoid space. It was assumed, however, that if a significant increase in intracranial pressure occurred under these conditions, it would be due

to a trapping of fluid in the ventricles and a diffuse hydration of tissue. The result of this would be that the swollen nervous system would respond as does one in which the continuity of the cerebro-spinal fluid spaces was interrupted by the presence of a tumour. In short, if the intravenous administration of hypotonic salt solution caused a significant amount of swelling of the brain, despite the fact that the cerebro-spinal fluid was allowed to escape during the injection, compression of the jugular veins would give the characteristic effect of "spinal block," with little or no output of fluid and little or no rise in pressure in a manometer attached to the lumbar needle. In no case was any evidence revealed of the existence of the condition of "block," the pressure or outflow responses being quite as prompt and extensive as before the injection.

This observation, while reassuring, was not perhaps conclusive. It is possible, however, to present at this time direct histological evidence of the absence of any hydration of the nervous system during forced drainage.

EXPERIMENTAL DATA.

The observations have been made on eight rabbits and four dogs under sodium veronal anaesthesia. The normal animals were taken in pairs of approximately equal weight, and to each pair equivalent or identical injections of hypotonic saline were given at the same rate. One and one half hours before the experiment each animal was anesthetized by giving 0.3 gm. Na-veronal intravenously, thereby producing a satisfactory and steady narcosis. In a few cases a whiff of ether was given at the onset of the experiment—and if this was done to one animal, it was also given to the other of the pair. Thus, each pair of animals was subjected to identical treatment, except that one animal was given the injection without allowing the cerebro-spinal fluid to escape, while in the other animal the cerebro-spinal fluid was allowed to flow freely from the cisterna magna, both before and during the administration of the hypotonic salt solution.

Immediately after the injection, and still under deep anaesthesia, the brains and cords were exposed widely in their bony framework, as far as possible avoiding injury to the dura. On exposing the medulla the animal died. The central nervous system in its bony skeleton was rapidly freed from the rest of the body and then immersed in 10 per cent. formalin. The formalin was made up in saline of the same strength as that which had been injected during the experiment. In

some experiments symmetrical blocks were also cut and placed in Zenker's fluid. Intravascular injections of fixative were not given for fear that the pressures used might introduce post-mortem deformation; and perfect cytological fixation was willingly sacrificed for the sake of the preservation of the relation of parts. The sharpness of the contrasts obtained seems to justify the method of fixation chosen.

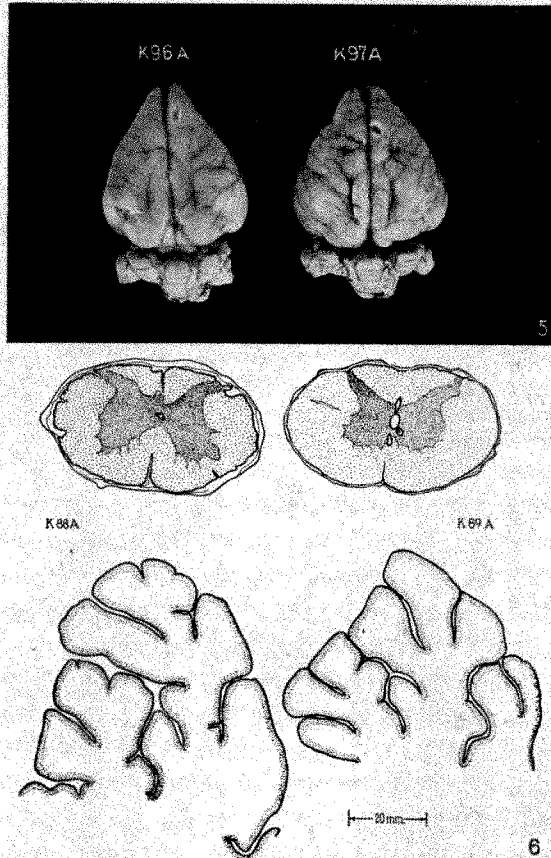


FIG. 5.—K96A and K97A, described in protocols and in text. Contrast between the swollen brain of the undrained and the normal appearance of the drained animal.

FIG. 6.—Contrast between the deep hydration of tissues in the undrained animal and the lack of hydration in the drained animal (see text and protocols).

RESULTS.

The contrast between the animals which had been drained and those which had not been drained could be clearly made out, both on gross inspection and under the microscope.

In fig. 5 the dorsal surfaces of the fore-brains of two rabbits are

shown. The brain of the undrained animal is immediately recognizable by the swollen, rounded, forward poles, the full sides, and the occipital poles which bulge so markedly as to hide completely the underlying corpora quadrigemina.

In fig. 6 is reproduced an exact camera lucida (Edinger apparatus) tracing from another pair of rabbits. Here the spinal cord of the undrained animal is so swollen as to fill almost completely the dural sac, the fissures and furrows are nearly obliterated, the central canal is ballooned out, and fluid-filled spaces are seen in the dorsal and ventral median fissures, while the mouths of the fissures are occluded at

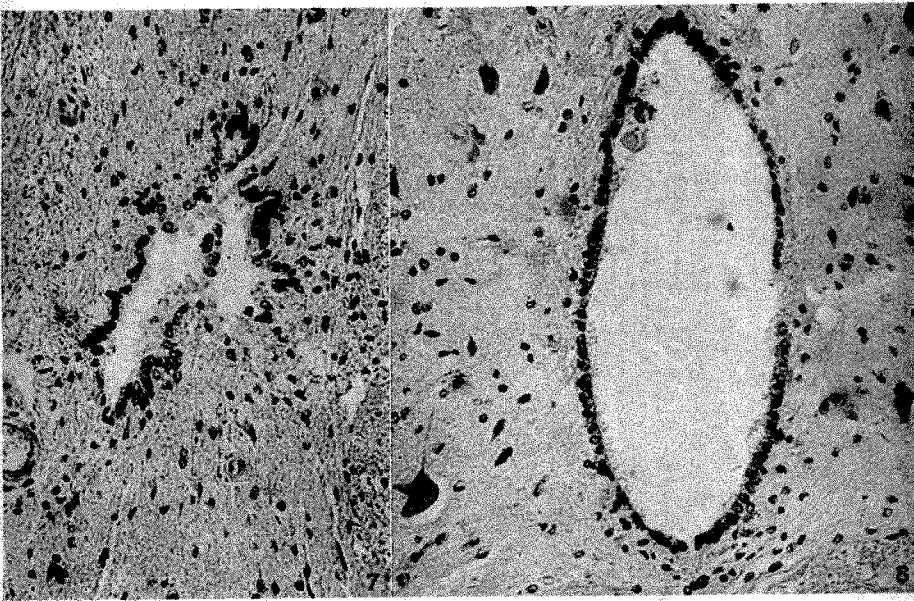


FIG. 7.—Undilated centra canal from drained animal, K88A. $\times 300$.

FIG. 8.—Tremendously dilated central canal from undrained animal, K89A. $\times 300$.

the surface. In contrast to this, the cord of the animal which was drained throughout the injection lies loosely in the dural sac, the periphery is dented by deep fissures, the central canal is small and folded, and no deep collections of fluid can be seen.

Similarly, the cerebellar sections show distinct differences. The section from the undrained animal is flattened at the surface, with occlusion of the mouths of the sulci, and fluid trapped in the depths; whereas the other has rounded folia and widely-open sulci.

In figs. 7 and 8 the contrast between the central canals is shown at

greater magnification, demonstrating the large distension of the one, while there is complete absence of any such deformation of the central canal in the cord of the drained animal.

In figs. 9 and 10 the great dilatation of the perineuronal spaces in the grey matter of the spinal cord is seen in the rabbit which was not drained (fig. 10), in contrast to the lack of any such dilatation of these spaces in the other (fig. 9).

The pictures presented here of the hydration of the tissues of the central nervous system as a result of the intravenous injection of hypo-

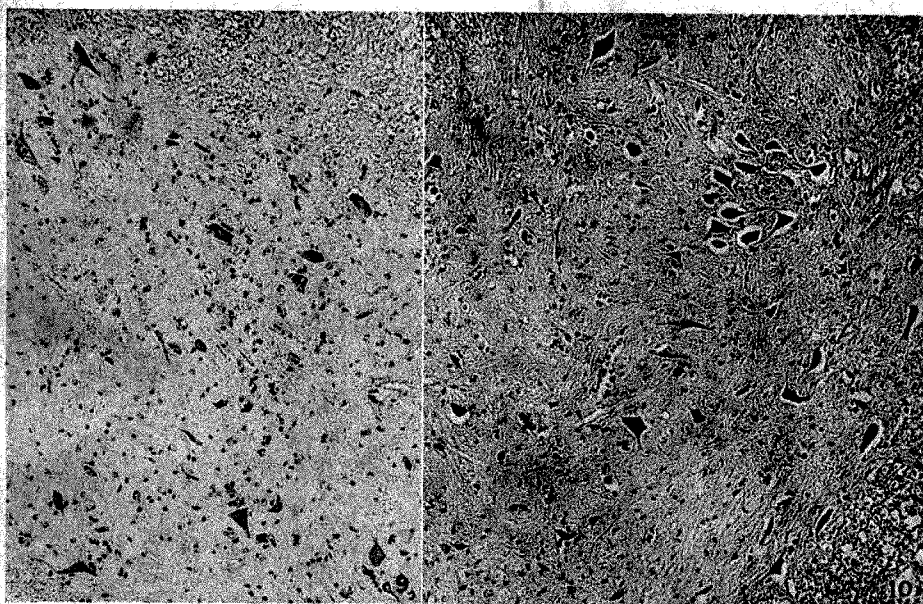


FIG. 9.—Undistended perineuronal spaces from drained animal, K88A. $\times 140$.

FIG. 10.—Tremendously distended perineuronal spaces from undrained animal, K89A. $\times 140$.

tonic solutions with the cranio-vertebral cavity intact, confirm completely the findings of Weed [4]. Similarly, these observations agree with his statement [*loc. cit.*, p. 271] that, "It is doubtful whether the nerve-cells themselves participated in the process."

Furthermore, when Weed and McKibben [5, pp. 541 and 545] compared these effects with those produced by similar injections which were given after making extensive openings in the skull and in the dura, they could find no evidence of such hydration in the animals with open crania. The present studies have shown that it is not necessary

to make any such wide decompression in order to prevent hydration of the nervous system, but that under the experimental conditions it can be equally well achieved merely by a continuous drainage of cerebro-spinal fluid. That there must be some limit beyond which the brain will swell faster than the fluid can escape would seem to be certain, but the studies so far completed have not established where this limit lies.

Finally, in figs. 11, 12, and 13, it is shown that the same marked contrast exists in the picture of the choroid plexus. The plexus from

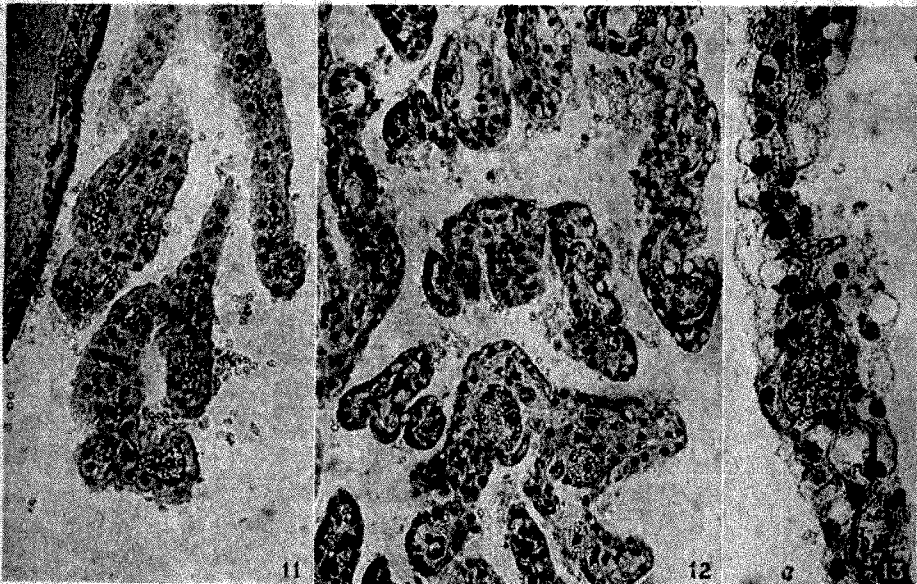


FIG. 11.—Unvacuolated choroid plexus from the drained animal, K88A. $\times 300$.

FIG. 12.—Vacuolated choroid plexus from the undrained animal, K91A. $\times 300$.

FIG. 13.—Vacuolated choroid plexus from the undrained animal, K 89A. $\times 510$.

the drained animal shows no vacuolation; that of the undrained animal is swollen with huge, water-filled vacuoles. The significance of this unexpected contrast is not entirely clear, and hence the subject is being studied further. The finding suggests that it is not merely the passage of water through the plexus which produces the vacuolation, but rather a joint effect of this and of the increasing intraventricular pressure; or else that when the cerebro-spinal fluid is allowed to drain during the injection the passage of water from the blood-stream into the cerebro-spinal spaces takes place, not through the plexus alone, but more generally through all of the capillaries of the central nervous system.

PROTOCOLS.

	Weight gm.	NaCl solution injected	Amount in c.c.	Duration in minutes	Venous pressure		Cerebro-spinal fluid
					Before injection	After injection	
					mm. saline		
Rabbits—							
K88A ..	2,000	0.45 per cent.	250 c.c.	40	80	75	Drained
K89A ..	1,975	0.45 „	250 „	42	100	95	Not drained
K91A ..	2,000	0.45 per cent.	475 c.c.	30	75	105	Not drained
K92A ..	1,950	0.45 „	450 „	30	70	110	Drained
K93A ..	1,900	0.45 per cent.	250 c.c.	20	80	90	Not drained
K94A ..	1,900	0.45 „	250 „	20	85	80	Drained
K96A ..	1,700	0.35 per cent.	250 c.c.	25	80	78	Drained
K97A ..	1,750	0.35 „	250 „	25	95	85	Not drained
Dogs—							
K94 ..	13,300	0.40 per cent.	750 c.c.	55	—	—	Drained
K95 ..	10,200	0.40 „	650 „	50	—	—	Not drained
K98A ..	4,520	0.40 per cent.	450 „	65	125	120	Drained
K99A ..	6,800	0.40 „	650 „	60	110	125	Not drained

The injections were made from a calibrated Woulfe bottle which was kept at body temperature in a water-bath. A constant, measured head of pressure was maintained in a large pressure reservoir. The venous pressures were determined before and after the injection by connecting a small-bore standpipe manometer with the side-arm of a T-tube which was inserted in the rubber tubing which led from the Woulfe bottle to the animal. The manometer was filled with the injection fluid, the tubing from the Woulfe bottle pinched off, and the level at which the fluid from the manometer ceased to run into the animal's vein gave a direct determination of venous pressure.

It is important to note that such large volumes of hypotonic solution can be injected slowly without materially altering venous pressure. This indicates that when the injections are made slowly the excess fluid must leave the circulation almost as rapidly as the fluid is injected, so that little increase of blood-volume results and no great strain is placed upon the heart.

CONCLUSIONS.

(1) Under narcosis large volumes of hypotonic solutions can be injected into animals without materially raising venous pressure, if the injections are made slowly.

(2) *If no escape of cerebro-spinal fluid is allowed*, the injections give rise to a marked increase in intracranial pressure, and striking hydration of the central nervous system.

(3) The hydration is manifested to the naked eye by diffuse swelling of the brain; but sections show the fluid predominantly in certain well-defined places, i.e., the ventricles and central canal, the choroid plexus, the perineuronal spaces, and the perivascular channels. No recognizable hydration of the neurones themselves occurs, and relatively little diffuse interstitial oedema.

(4) *If free escape of cerebro-spinal fluid is allowed*, the injections produce little rise in intracranial pressure, and no recognizable hydration of the tissues of the central nervous system; i.e., the ventricles and central canals remain undistended, the choroid plexus is free of vacuoles, and the perineuronal spaces and perivascular channels are not dilated.

(5) It is evident, therefore, that lowering the osmotic pressure of the blood by the intravenous administration of hypotonic solutions causes a transudation of fluid from the capillaries into perivascular and perineuronal areas throughout the whole central nervous system; and that by simultaneously draining the cerebro-spinal fluid a free escape of this transudate is accomplished from the depths of the tissue to the surface through some pathway of least resistance (presumably the perivascular channels).

(6) In this way a washing-out of perivascular exudates into the subarachnoid space was achieved in experimental meningo-encephalitis in cats.

(7) The observations suggest the use of forced drainage as a means of treatment of certain infections of the central nervous system in man.

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THE CLINICAL DIFFERENTIATION OF PSYCHOGENIC AND PHYSIOGENIC DISORDERS.

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THE clinical differentiation of psychogenic from physiogenic types of illness is a common problem. Clinically there is a vast difference between bodily disorders which are of the psychogenic kind, and those which are clearly the result of physical disease. Between these extremes there occur many cases in which it is very difficult to decide, with the data available, between a physical and a psychic origin. It is with the purpose of defining more clearly the criteria on which differential diagnosis can be based that the following paper is written. It should be observed that the differentiation of physiogenic from psychogenic is not precisely the same as the differentiation of "organic" from "functional," for "functional" can be physiogenic. Further, it has to be remembered that in a given case the physiogenic and the psychogenic may be intermingled, but it is only with their differentiation that we are now concerned.

That the problem is a difficult one was evident during the war. Some clung to the hypothesis of a physical ætiology of "war neuroses," while others maintained the preponderating importance of psychic factors. The latter view prevailed, but some able neurologists continued to hold the opposite belief. Oppenheim [6], for example, upheld his theory of the origin of the "traumatic neuroses," which he considered were caused by "mental or physical shock, affecting chiefly the cerebrum and producing molecular changes in the areas which control the higher mental functions and the motor and sensory functions related to them." He also supposed that "fine organic changes" might exist in addition, as in the vessel walls and in the myelin of single fibres. Similarly, conditions described by some as "reflex paralysis," due to organic changes in the cells of the spinal cord [2], were elsewhere being cured by the ordinary methods of psychotherapy [3].

It is evident that such divergences of opinion must depend on difficulties of interpretation of the phenomena in question. These

include not only physical signs, but such data as the history of development of the signs and symptoms, and the patient's personality and attitude, to which much less attention is usually paid than to the signs themselves. It is the purpose of this paper to consider the behaviour of the patient and not merely the local bodily phenomena he presents, and to formulate, if possible, criteria which may be useful in arriving at a differentiation of the psychogenic from the physiogenic. The cases utilized for this purpose, presented for the most part certain unusual combinations, in consequence of which a number of them were diagnosed at different times in contrary senses.

Case 1.—Hairdresser's assistant, aged 26, female, single, was admitted to the Cassel Hospital in July, 1925.

The patient was the youngest of four siblings. Her father and a paternal aunt and uncle died of tuberculosis. Her childhood was healthy. She attended school from 4 to 15 years of age, leaving in the seventh standard to become apprenticed to a hairdresser. She liked the work.

In August, 1922, she gave birth to an illegitimate child. During the pregnancy she was greatly distressed and tried various abortifacients. At this time also she was knocked down by a motor-car. She explained she "could not move out of the way," and at the time "didn't care what happened" to her. Knowing herself to blame, she did not attempt legal proceedings.

Present illness.—After the birth she felt very weak. She could not bear to look at the child, whose arrival caused great antagonism to the mother in the household. The child was deformed, one side being smaller than the other. Refusing even to see the child, she had not observed the deformity for herself, and when informed of it three months after the birth she was much perturbed; it immediately occurred to her that the father must have had "some disease." (She had seen Brioux's play, "Damaged Goods.") On the same day that she received this information she observed a tremor of her left hand while at work. She forthwith began to conceal this tremor and used her left hand as little as possible. Presently she found she could not use it at all, and thought she had had a stroke. Later her left leg became weak. At first she thought her disability was on the same side of the body as her child's deformity, and was surprised to discover it was not so. Her doctor told her that the hemiparesis was due to the shock of hearing of her child's deformity. She was sent to a psycho-analyst, who told her that "something in her past" was responsible for her symptoms, and analysed her dreams, giving her frank sexual interpretations. She fell in love with the analyst, but promptly recognized this and broke off the treatment. Electricity and massage having also failed she was sent to hospital.

Closer inquiry into her history revealed that following the birth she felt drowsy, saw double, could not walk straight, and had dribbling of saliva. She saw "snakes and lizards" out of the right corner of her eye, and though she

knew they could not be real, this annoyed her. She had to resign from her work because she became slow.

From this history the plausibility of a psychological explanation of what proved to be an organic condition was so great that she was informed by physicians that her illness was psychogenic and was treated accordingly. Further, she stated that during pregnancy her left side had twitched, and that she had seen a woman with a hemiplegia reputed to have followed parturition, and had wondered whether she herself would be like that. She had attributed the twitching to the abortifacient drugs she had taken, or alternatively to the pressure of the foetus on some nerves. The auto-suggestive potency of such speculations in her then highly emotional condition seems at first sight great. The chain of psychological evidence seemed fairly complete. Her relatives, who had been unsympathetic, were now repentant of their attitude. Her illness had gained for her the sympathy she craved. If there be a flaw, it seems to lie in the clearness of the connection that existed in the patient's mind between her idea of the origin of her child's one-sided deformity and the tremor of her own left hand. There is also the fact that she was reluctant to take advantage of her illness by leaving her work, and if she gained sympathy by it, she also felt very keenly her loss of employment, and was very reluctant to accept it. Her mental attitude would have been in a hysterical patient unusually frank and receptive from the start of treatment.

There were, however, apart from the physical signs certain facts that did not fit with the hypothesis of a psychogenic origin. Thus, she was made to resign from her work, having clung to it after she was much disabled physically; she gave important associations with ease, and she accepted the psychogenic explanation with avidity.

Although her condition was not that of an ordinary hemiplegia, as the plantar and abdominal reflexes were normal, there were signs that could not be hysterical in origin, as irregularity of the left pupil and sluggish reaction to light—although Janet [3] has described "hysterical" conditions of this kind; "lead-pipe" rigidity of the limbs, especially of the left arm; immobility of posture and slowness of all her movements, and slight facial immobility. In other words, the physical signs suggest an extra-pyramidal lesion. The history of diplopia and other symptoms indicated that they were the residuals of an attack of epidemic encephalitis, but as she had a strongly positive Wassermann reaction in her blood, the possibility of a syphilitic thrombo-endarteritis must be considered. The cerebro-spinal fluid was normal.

Mental status.—There was no peculiarity of behaviour other than the slowness of her movements, and some mild erotic tendencies. Her mood was labile; as a rule she was happy and laughed readily, but occasionally she was mildly depressed. Sometimes her phases of depression occurred without reason, at other times in response to external circumstances, e.g., once she contemplated suicide as a solution for her difficulties. Her principal concerns were her health, her work, and her mother's attitude. She was very desirous of getting well. There were no longer any hallucinatory experiences. Orienta-

tion, memory, recent and remote, attention and comprehension, were intact. Simple calculation was badly done. Her Binet-Simon rating (Terman) was 12 years 8 months.

Course in hospital.—She was easily persuaded that her disability was in part functional, and re-education at once produced an improvement in her gait. Improvement in the movement of the left arm was slow and slight. Antisyphilitic treatment was given, but without result.

Comment.—The history of visual hallucinations, with insight, is interesting, especially in the light of a recent discussion [7]. They are unusual in epidemic encephalitis. Their occurrence in this case suggests the query whether it is possible for an affection of the lower optic centres in the thalamus or in the mid-brain to give rise to hallucinations.

The motor "accident," as a suicidal attempt, is of some medico-legal interest, especially as it bears on the question of the psychogenesis of impulse. Here the impulse, as is usual with impulses so-called, came out of an abnormal setting. The wish to die was present, and actually in consciousness when the opportunity presented itself.

But the interest of the case lies principally in the plausibility with which a psychogenesis suggested itself, if the physical signs were neglected or misinterpreted.

That the direct sequence of symptoms upon some moving incident does not speak by any means invariably for the emotional origin of these symptoms was still more clearly shown by another post-encephalitic patient who had, to the best of his knowledge, recovered completely from the acute stage, and who continued to feel well until one day the auditors of his accounts found a trifling deficit in his cash-book. He immediately began to "shake all over" (he had not had tremor at any time before) and to feel very weak. From that date his weakness increased, and he observed significant changes, especially a slowness at his work. He recovered sufficient confidence to return to work for a time, but again felt tremulous and weak when his assistant left him and he had to work alone. He then gave up work, and when he came under observation a few months later he had a well-developed Parkinsonian condition.

The same patient exhibited another aspect which was directly opposed to what is commonly found in psychogenic conditions. He doggedly believed in the purely mental basis of his symptoms and physical disabilities. This is so contrary to the usual attitude of the psycho-neurotic, who is strenuously seeking an honourable physical

excuse for himself, that it should at once excite a suspicion that the condition in question is of physical origin. Both attitudes—that of the post-encephalitic Parkinsonian patient referred to, and that of the psycho-neurotic—are, of course, the outcome of the patient's wish to hide the truth from himself.

In both the patients already cited, a psychogenic origin had been presumed at one time or another. It is more common to encounter patients in whom an organic disease has been diagnosed, when only psychogenic symptoms are present. An unusually clear example of the latter contingency occurred in Case 3.

A man, aged 60, presented himself at the out-patient department of a psychiatric clinic and was diagnosed as general paralysis. It is true that he complained of loss of memory, that he had a marked speech defect, that his gait was ataxic and his writing scrawling, and that his blood Wassermann was positive. But even a mildly critical examination of these signs and symptoms alone, apart from a routine neurological examination, which revealed nothing, showed that the patient, besides being depressed, was extremely anxious about his condition, which is unusual in general paralysis; that his speech defect was inconstant, not being always present and sometimes being a stutter, and sometimes slurring; that only the form of his handwriting was changed; and that his gait was of a stumbling and not of a truly ataxic kind. Furthermore, a little investigation revealed previous attacks, and that the patient, who had been chairman of an asylum committee, had read Mott's "Archives," and knew that he had had syphilis. Finally, his cerebro-spinal fluid was negative in all respects. But his case emphasized the necessity of examining more minutely the nature of physical signs themselves, and the unexpected light which even a superficial mental exploration may throw on their anomalies.

The following case affords some problems of a kind somewhat different from those presented by the previous patients, but likewise concerns the relationships of physical signs and psychical disturbances. Like the two preceding cases also, it had had attached to it a "functional" diagnosis, with a presumption of a psychological basis.

Case 4.—Architect, aged 53, male, single, was admitted to the Cassel Hospital in September, 1925, with the following report:—

"One has a feeling of doubt whether there is an organic element in his condition. The main point of interest in our examination is that he has a well-marked hyperchlorhydria. As soon as a trace of bile appears in the wash-out (when his stomach is washed out because of a complaint of discomfort), he expresses himself as relieved. This is probably almost entirely mental, as it is his conviction that excess of bile is at the bottom of his condition. Radiographs show no abnormality of any kind. A disconcerting feature is the

frequency of occult blood in the stools. Although he has hyperchlorhydria, this cannot itself be responsible for his symptoms, which must be very largely psychogenic, for he is not suffering from any serious organic disease." He complained of "terrible acidity and terrible depression."

Family history.—He was the second of a family of seven, of whom two died in infancy, one of convulsions, and the other of whooping cough. There was no other history of nervous or mental disease.

Personal history.—The only neurotic trait admitted in childhood was stuttering. He left school at the age of 17, having reached the highest class. Soon after leaving school he took up architecture, going abroad at the age of 30. While abroad he had "fever" for three months in 1914. During the war he was employed on war-work in this country. In 1919 he returned abroad, and then was in the midst of civil and military disturbances of all kinds, without actual bodily harm to himself.

He evidently was an unusual type of personality. A conscientious worker, without ambition, he denied any tendency to worry, or any habit of attending to his aches and pains. No sort of sexual urge was discoverable in him. He was sociable and extremely talkative, but a total abstainer. Dim light had a depressing effect on him.

Present illness.—His "acidity" began when he was about 18. He thinks he first noticed it on waking from a sleep in the office on a slack afternoon. It consisted of a burning pain in his abdomen, and of heartburn, which was relieved by bismuth. He denied any depression or any interference with his work at that time. The "acidity" became worse during the war, accompanied by a few transient depressive episodes which he attributed to irregular meals. After the war they became more severe. In the last few years he has had regular cycles of acidity, depression and relief, every few days. Relief always followed the vomiting of bile or of acid. He described this depression as a feeling as if "everything were sinking below" him, and as if some terrible catastrophe were about to happen. It has always been worst in the mornings and lasted for about an hour only. While he was abroad his symptoms did not occur at times of excitement, e.g., while in the neighbourhood of a riot. He felt that all the time he was in foreign parts he was in a state of tension, and that danger steadied him. Latterly it was an effort to start work. Insomnia for several nights in succession accompanied the cycle of symptoms. He denied that his symptoms occupied his attention excessively, but he regarded them as a nuisance.

Physical status.—He was of medium height and "pyknic" habitus. Neurological examination was negative. There was chronic otitis media in the left ear, with cholesteatoma and polypí. There was some gingivitis. Gastric juice: during an attack of acidity, three hours after breakfast, the free acid was 0.29 per cent., and the total acidity 0.34 per cent. X-ray showed no abnormality, but there was occult blood in the stools in eight of thirteen examinations. The Wassermann reaction in his blood and cerebro-spinal fluid was negative. The other systems were normal.

Mental status.—He was very talkative, with much circumstantiality, and very active. There was no slowing. There was no apparent depression on admission; indeed, there was little evidence of depression at any time, beyond the subjective complaint of it. At these times he was rather less active and did not talk with so much animation. There was no disorder of thinking, subjective or objective. His only concern was his health, and he did not insist upon it, readily talking about other topics, and even preferring them.

Course in hospital.—He complained of symptoms of hyperchlorhydria at varying intervals, lasting a few minutes to several weeks. They were always accompanied at one time or another in their course by a feeling of mild depression, but never gave rise to more than slight objective evidence. Depression did not occur apart from the periods of hyperchlorhydria. The latter began sometimes in suggestive circumstances, as when in the train on his way to consult an aurist, but on most occasions there was nothing to suggest a psychic precipitating factor. He took the symptoms of acidity in a matter-of-fact way, without special concern, but attempted to get rid of them by treatment. He considered that his depressive episodes would continue longer if he allowed them to do so, and claimed that he cut them short by engaging whole-heartedly in occupations and games. After three months in hospital he remained entirely free from symptoms of any kind.

Following a radical mastoid operation, he presented an interesting series of reactions. He complained bitterly of a severe "neuralgic" pain all through his head, and said that he slept practically not at all for weeks afterwards, in spite of morphine. He was at this time in a nursing home, and not under our direct observation. The wound healed well, but for six weeks after the operation he preferred to spend most of his time in bed, saying he was too weak to move. Nevertheless, he had no return of the hyperchlorhydric symptoms or of frank depression.

Comment.—The interest of this case lies:—

(1) In the fact that the patient's complaints were attributed, after careful general medical investigation, primarily to a functional and presumably emotional disorder, and that it was considered that "organic disease" could be excluded.

(2) In the relation of hyperchlorhydria to emotional disorders; there was a very close association of depression with hyperchlorhydria.

(3) In the possible rôle played by physical disorders in producing disturbances of mood. In this instance the depressed mood might be considered either: (a) as a psychological response to the discomfort of hyperchlorhydria; (b) as the direct result of an intimate relationship between the physical basis of hyperchlorhydria and the frequently assumed physical or "metabolic" basis of depression; or (c) as the cause of the hyperchlorhydria.

In favour of the depression being the consequence of the secretory

disturbance is the fact that the latter had begun many years before any depressive episodes were admitted, and that under our observation the depression did not seem to occur apart from periods of hypersecretion. That depression was associated with the later attacks only would perhaps be explained by the factor of increasing age, with consequent diminution in external interest, especially since the patient had always had a singularly limited outlook. On the other hand, his attitude to his symptoms was not at all hypochondriacal, as such a hypothesis would almost seem to demand. The difficulties of life abroad may have been a considerable factor, and were of a type likely to work psychologically rather than physically. His subjective account of "tension" and the disappearance of all his symptoms when his interest was sufficiently aroused speak for this.

It will be seen that the questions arising are much involved. The long history and the absence of discoverable psychic factors in the beginning, and especially the presence of occult blood in the stools, would seem to be decisive in favour of an organic lesion. The absence of pain, the lack of a definite relation to the time of taking food, and the negative X-ray findings do not support this, however.

One is tempted to conclude that there was organic disease present, and that with the superaddition of such factors as advancing age and disturbed conditions of work, mental symptoms, especially depression, appeared. But the depression was of a singularly automatic kind. After lingering for weeks on one occasion, the acidity and depression disappeared suddenly while he lay awake at night. He felt he could locate exactly the point of time when they left him—suggesting a direct connection of hypersecretion and the physical basis of depression, rather than a relationship via a psychic route. The behaviour after operation, with substitution of a persistent "neuralgic" pain for the previous symptoms which remained in complete abeyance, is, however, again suggestive of a psychopathic predisposition from which functional symptoms would readily arise.

The following case, which was a straightforward anxiety-state, is given briefly, not because there was any difficulty in its diagnosis, but because it affords some fruitful contrasts to the first two cases, and to the next.

Case 5.—Aged 43, male, labourer, married, was seen in the out-patient department of Guy's Hospital, in January, 1926, with a complaint of tremor of his head and legs, headache, and aching in his legs.

Family history.—He was the second of seven siblings. A sister became

depressed at times. His father, who was alive, aged 71, had been depressed for years and suffered from "neuritis." The patient had no children.

Personal history.—The patient denied neurotic traits in childhood. He was an average scholar, and got on well with his fellows, but was quiet and rather timid. Appendicectomy was performed in August, 1914. He did not volunteer for service, but was called up several times and on each occasion rejected. He married, when he was 41, a woman of 39. She was a quiet, sensible person, who did not "nag" him.

Present illness.—In August, 1914, he felt "queer," became afraid that something was going to happen to him, and began to tremble. He complained of abdominal pain, had an appendicectomy done, and experienced no more tremor at that time. Tremor recurred, however, when he was called up for an Army medical examination. He was classed C 1 and sent back to his work. The tremor disappeared till he was again medically examined, and was again sent back to work. This time the tremor did not reappear till November, 1923. From that date it became continuous, and gradually increased. He thought about it a good deal, and wondered whether it would ever leave him, and he had become so worried about himself that he gave up work six weeks before seeking advice at the hospital.

Mental status.—He was a quiet, meek-looking man, who seemed mildly depressed, but smiled readily. He complained, in addition to the tremor and aching, that his head was "muddled," that he was depressed, that his thoughts seemed slow, and that his memory was poor. Objectively there was no retardation and he retained seven digits. His only concern was his health. There were no delusional trends and no sensorial disturbance. His general intelligence was fair. He was pallid, fairly well-nourished, and had a dorsal kyphosis. The knee-jerks were slightly exaggerated, but there was no evidence of any organic disease.

Progress of case.—In the same interview in which the above history of the previous attacks of tremor was obtained, he denied any financial, marital, or occupational difficulties at the time of the recurrence of the tremor in November, 1923, but finally, in response to the general question, "Did anything at all occur to you in November, 1923?" he thought for over a minute and then said, "Why, I got married then." It appeared that he had felt that marriage was a great responsibility, that he had been a little afraid of it, and had begun to tremble as the occasion approached. He had trembled ever since.

The coincidence was so striking that even the patient saw the humour of it. He returned to work the following week, his tremor having disappeared, and was asked to report if he had any recurrence. He has not reported.

Comment.—This case shows some points with unusual clearness.

(1) The direct relation of mental content to the existence of physical sign, both conscious in themselves, was not realized by the patient. It was the connection between them of which the patient was unaware (cf. Ross [8]). In this respect the case forms an interesting contrast to

Cases 1 and 2, in each of which the patient was fully aware of the immediate temporal sequence of content and symptom. It seems that where the patient himself gives from the beginning a plausible association between content and symptom that the latter is suspect of a different origin, which may, of course, still be psychogenic, but from a different mental source.

(2) The persistent physical signs were of the type directly producible by an acute emotional state (fear in this case). An immediate sequence of emotional disturbance and physical sign is, of course, very suggestive of a causal relation between them. From the case at present under consideration, it would seem that a physical sign persisting long after the occurrence of the original psychic trauma is likely to be of psychological origin, provided the physical sign is of the kind regularly produced by emotional disturbance, and provided the connection between emotion and sign is unknown to the patient from the beginning, or forgotten by him. But such an assumption was made in the following instance, and the patient had been informed that he was suffering simply from "nerves."

Case 6.—Male, aged 54, was admitted to the Phipps Psychiatric Clinic, Johns Hopkins Hospital, in February, 1924, complaining of paroxysmal palpitation which disabled him for work. His wife complained that he took undue care of himself and lived in constant apprehension of his heart attacks. He was the youngest of a family of six. One brother "went to pieces nervously," but recovered. The patient has three healthy children, the eldest aged 21.

Personal history.—He was always healthy. At the age of 19 he left high school and went to a university for a year. He then went into business, and married at the age of 32. For some years he had been in the habit of drinking whisky three times a day on the average, and about two ounces at a time, in order to combat a tendency to become fatigued.

Personality.—He had always been sociable, happy, talkative, and over-energetic. His wife, on their first meeting, thought him the "most nervous man" she had ever seen; he was constantly active, laughing, talking and joking. Never until his present illness did he give any thought to his own health, which was always apparently excellent.

Present illness.—The patient had had a feeling of nervous shakiness for an indefinite time (some years). In December, 1922, or thereabout, he began to have a dull feeling in his chest, especially after exertion, sometimes amounting to actual pain. In March, 1923, following a certain amount of emotional disturbance occasioned by his eldest boy's leaving home and by his wife's consequent distress, he suffered from nausea and diarrhoea. In the morning his wife accidentally observed that his heart was beating very fast and

pounding against his ribs. The patient himself had noticed nothing of this. A doctor was called in who, knowing of his over-active disposition and his alcoholic habits, tried to scare him into taking greater care of himself. He succeeded so well that the patient had rarely done a whole day's work since.

Attacks of palpitation occurred at intervals of about two weeks during the eleven months preceding admission to hospital. They were usually brought on by exertion, and especially by fatigue, which supervened more readily than before his illness. The attacks, which were accompanied by diarrhoea, varied in duration from two to twenty-six hours and left him very tired. He always lay down during an attack. He had lost weight.

Since the beginning of his illness he lived in the fear of precipitating an attack, and of a possible complete disablement if the palpitation should become permanent. To avoid this catastrophe he limited his activities, both in work and recreation. He frequently counted his pulse and observed his cardiac pulsations in a mirror. When an attack came on he lay down, no matter where he might be. He once lay down on a city pavement, and was soon surrounded by an inquisitive crowd. On his doctor's advice, if an attack came on in his office he immediately took a taxi home. His attention to his business suffered in consequence. He moved his domicile to within two blocks of his office, but even this proximity did not reassure him, and he frequently returned home. His friends, observing no special change in his appearance and no apparent reason for his complaints, insinuated that much, if not all, of his trouble was mental.

Mental status.—He was an intelligent, co-operative patient. No sensorial defect, and no subjective or objective failure of memory, thinking or attention, were evident. His reactions were all rapid and he laughed and joked in a forced way. He discussed his symptoms intelligently and in considerable detail, and he frequently felt his pulse during an examination. He stated that he had considerable fear during the attacks of irregularity lest the irregularity should become permanent and decompensation set in.

Physical status.—He was a thin, sallow-complexioned man, and of poor muscular development. His activity was of the "nervous" type. Even in ordinary quiet conversation a tremor of face and hands was evident, and as he lay in bed he threw off the bed-clothes because he felt too hot.

His pulse was rapid, 102 in the recumbent position, and there was an occasional missed beat at the wrist. For one period of twenty-six hours there was total irregularity, 98 at the apex and 92 at the wrist. The heart dullness did not enlarge during this attack. An electrocardiogram taken during the period of irregularity showed irregularly spaced and additional pulse waves associated with pulse waves of irregular amplitude.

There was fine tremor of the facial muscles, tongue and fingers. Von Graefe's sign was present. There was a swelling in front of the lower part of the trachea, and on either side of the mid-line, especially on the right side. It moved with swallowing, was rather firm in consistence, and showed no pulsation. There was a systolic bruit over it. The basal metabolic rate was + 29.

Course in hospital.—The patient was operated on, and the left half of the thyroid removed. It was found to contain toxic-adenomatous masses. His recovery was uneventful, with the exception of one recurrence of palpitation in the first few days following operation. He returned to business and a year later reported that he was in excellent health, had had no recurrences, was putting on weight, and was free from anxiety.

Comment.—The case is of service as a control of our other observations, in that emotional factors seemed to play the preponderating part in what proved to be an organic or structural disease. In the first place, the patient's personality was that of a "very nervous," i.e., restless and emotional, man. Secondly, the first symptom followed almost immediately on a moving incident, although he did not himself associate his palpitation with the incident in question; and thirdly, a state of unceasing anxiety about his condition was punctuated by the occurrence of attacks of palpitation, which on general psychological grounds were to be expected in these circumstances. This is, *prima facie*, the behaviour of a psychogenic illness. But in his mental attitude there were aspects which suggested a different explanation. The first attack of more forcible heart action was observed, not by himself but by his wife; although anxious between attacks, he was not depressed, but fairly cheerful and laughed readily; and his anxiety was accompanied by a kind of subjective certainty which precluded reassurance. Yet it was not an anxiety of the almost obsessive-thinking kind, for it did not exclude other interests. The physical signs and the cessation of anxiety after operation established that the illness was primarily physiogenic. But from the history alone a psychological basis seemed more likely.

The case illustrates once more the fact that to argue even from striking coincidence of psychological and physical events, and also from general grounds of personality, is fraught with some dangers.

Such coincidences come the more frequently under observation the more we pursue parallel historical investigations into physical and psychical conditions, and difficulties of diagnosis consequently arise where they would hardly otherwise have been suspected.

Case 7 came under observation at the age of 35, and was in an extremely anxious state of mind, complaining not only of constant palpitation and weakness, but of fears of trains and of heights. He was sent for treatment on the assumption that his condition was primarily a psychogenic one.

The early history of the palpitation seemed to favour a physical origin; it followed immediately on an attack of influenza seventeen years before. He disregarded it to the extent of playing games as before, and was surprised when

his climbing ability became limited; it improved many years afterwards, while his mental distress on apparently other grounds was increasing. Further, the palpitation improved for a time after a partial thyroidectomy, and he gave up *successful* work on account of it.

If one substitutes the general term "disabling physical symptom" for "palpitation," this can very well be the account of a struggle against increasing physical disabilities. But palpitation is a symptom more commonly produced by emotional than by physical causes, and if the subjective conditions be considered there were coincidences that were at least suggestive. The patient's palpitation began at a time when he was making an effort at sexual suppression. Further, it attracted his close attention when his private affairs had met with disaster. In this connection his persistent attention to his cardiac symptoms would doubtless be construed by some as an attempt at excusing himself for the failure of his ambitions.

Moreover, the development of obvious anxiety some years subsequent to the beginning of the palpitation might be said to be simply the long-delayed overt appearance of what was always a strong underlying trend.

In such a case it is evident that while in the manner of unfolding of the apparently physical symptoms there is nothing that is characteristic of anything but physical disease, inquiries along other lines reveal impressive coincidences of psychological events with physical phenomena. Merely on the ground of coincidence to attach a causal signification to these events would not be wholly justifiable. There often are other grounds, however; in the case now being considered, the anxious mental attitude to the palpitation was a part of a more general anxiety; the patient had an admittedly neurotic make-up, of which the present acute anxiety was simply a further development. But it may be objected that palpitation of emotional origin would not last, as this man's did, for eighteen years, in the absence of a continued cause. If *a posteriori* conditions are allowed weight, then in favour of an emotional origin of palpitation is the fact that it obtained for him immunity from work and a life of indolent ease. It is true that he latterly stated with much emphasis and apparent sincerity that he would infinitely prefer to be healthy and at work. Since the pathologist's report of a portion of thyroid removed at operation held that toxic goitrous changes were present, the conclusion that had finally to be accepted in this instance was that both physical and psychological factors were at work.

Illnesses, which, like the one just commented upon, begin with

obvious physical traumata, as infections, wounds, blows, &c., as be accepted by physician and patient alike as having a physical origin. This has been notoriously the case in the past; for in the theory of the war-neuroses already alluded to, and in the "work" theory of the ætiology of "neurasthenia." A similar acceptance of physical coincidence was also responsible for some former absurdities of psychiatric classification, when near physical disease had its particular type of insanity attached to it, a tendency to attribute everything to the physical trauma, inflicting whatever the noxious agent was, becomes all the stronger when the patient strenuously denies any mental perturbation at the time. For example, a young farmer (Case 8), who complained of palpitation and attacks of faintness, had his first attack at the age of 19, after severe manual labour under a hot sun. The second attack occurred at a similar circumstance. In the intervals he was so far from showing any apparent anxiety that he disobeyed his doctor's orders as to rest and of activity (e.g., in cycle trials). But the lack of anxiety was more apparent than real, for while he denied its existence between attacks, it became very apparent in hospital on the occurrence of feelings of malaise, as when he ventured into the neighbouring town. His sedentary activities had, in fact, become more and more governed and controlled by the knowledge that he was subject to such attacks. It seems that some actual physical over-exertion produced palpitation to which the patient paid too much attention, and which formed the point of a long succession of anxiety attacks. This is scarcely sufficient to establish the purely emotional basis of their continuance, and the suance of other lines of inquiry soon seemed to justify the assumption of a psychogenic basis. This lay: (a) in his upbringing as a child by an anxious mother, who had herself, to the patient's knowledge, suffered similar attacks; (b) his unexpressed rebellion against his father's design for his career and the general dissatisfaction with his work arising from this; (c) a keen feeling of social inferiority which he entertained; and (d) his concern over masturbation. Furthermore, his personality was of the dependent, unenterprising type, and consequently not equal to handling his difficulties frankly and for himself.

If it is sought to fulfil another "canon" of psychogenesis, that an object is fulfilled by illness, it might be said with some plausibility that his illness proved to himself and his friends his unfitness for farming which, as it proved under a modified analysis, he

disliked. It is true that the unfitness extended to things which he liked, as dancing to a late hour; but this is an illustration of the all-or-none character of emotional reactions in general, which distinguishes them from the narrow "situative" reactions which Kretschmer [5] stigmatizes as simulations.

When the rôle of physical agents in the causation of certain symptoms is further considered, the *latent period* which often occurs between the incidence of the trauma and its apparent effects becomes a matter of some importance. Babinski and Froment [1] maintained that during the war hysterical manifestations were practically unknown during or immediately after traumatic experiences, i.e., they were rare at the front line in the war, but common in clearing stations and at base hospitals. Kinnier Wilson [10], in a recent paper, has illustrated the difficulties and pitfalls in assuming the relation of trauma to subsequent organic nervous disease. The task in the case of psychogenic nervous disorders is perhaps easier, since theoretically at least it is possible to recover memories of the latent period, and to reconstruct the general mental condition of the patient at the time of the trauma. Nothing analogous to this can be attained in the case of essentially organic lesions.

The following case illustrates this latent period and the nature of its content very well. The great majority of the symptoms presented no difficulty in differentiation from physical disease, being obviously of a hysterical or simulated kind; but if there was any doubt about a possible injury to the musculature of his back, it was dispelled by the obvious significance of the psychological factors concerned. This case also throws some light on cognate questions of differential diagnosis from organic disorder.

Case 9.—Male, aged 50, married, a spinner by occupation, was admitted to the Cassel Hospital in July, 1925, complaining of difficulty in walking and inability to use his arms, chiefly the left, as well as formerly, following an accident two years before admission.

Family history.—Patient was the oldest of five siblings, of whom the fourth was alcoholic and had died. Patient's father died at the age of 75, just before patient's accident; he had received an injury to his foot from a horse and "went to pieces" after it.

Personal history.—The patient had been a mill-worker since the age of 10. He denied having had a day's illness in his life except as the result of an accident twenty years before, when he had a "strain in the groin" which kept him in bed for three months. He recovered completely and refused compensation, having been advised to do so on the ground that if he had accepted it and the trouble had recurred he would have had no further claim.

He drank beer, but not to intoxication as a rule. He was a good workman.

Present illness.—Two years and four months before admission, while on a ladder putting a belt on a driving wheel, he was "twisted round" to the right and "felt something breaking in his back." A fall from the ladder might have meant laceration by the machinery and he was very much frightened by the accident, trembled, and had to sit down, "because his legs felt weak." Just then an overseer passed by, spoke to him and made light of the accident, even laughing at him. This made the patient feel aggrieved, especially as he could not retaliate from fear of losing his job. He continued at his work the same day and for two days following, excepting a Sunday which intervened. The weakness and trembling continued at intervals during these days, so that he felt obliged to have his son to help him. On the fourth day after the accident, when nearing home on returning from work, a "pain struck him in the back" and he fell down. He crawled home on hands and knees. He observed nothing the matter with his legs and arms at that time. One doctor after another examined him at the request of his Union, and all gave negative reports. He did not improve, however, and "got tired of going to doctors." He remained off work on a compensation allowance. Eighteen months before admission, while drinking tea his right hand began to shake and he let the pot fall. He "wondered what was the matter," and his arms and legs had felt weak ever since, the weakness gradually increasing. His legs felt dead sometimes and he had to force himself along. Irritability developed "as if someone has insulted me." Gradually his sleep diminished; he had difficulty in going to sleep, and woke up often. He had become "tired of living" and would have liked at times "to lie down and die." His memory had been bad ever since the accident. He went among his friends saying that he "would never work again," and they sympathized with him.

From the time of the accident he was on compensation, which was 35s. a week less than the amount of his earnings. He came for treatment on the understanding with the employer's representatives that if he did not get well there he would be considered a "hopeless case," and would receive a lump sum of about £500. His job had been kept open for him.

Mental status.—His expression did not betray any special affect as a rule, but occasionally he wore a miserable expression. He said that sometimes he was very depressed, and had even a feeling of guilt at times "as if I had done wrong to somebody." Apart from his gait there was nothing abnormal in his behaviour. There was no retardation and no disorder of thought. His topics were his symptoms. He believed he was "breaking up" like his father. He denied financial worry, or any desire for compensation, declaring he would much rather be well and able to earn his wages. But he declared at one interview that he would set himself up in business with the lump sum which would be his settlement, and at another that it would be of no use to him. His memory was subjectively "awful," but no objective defect was demonstrable except for the psychogenic explanations offered to him to account for his illness. These he invariably forgot completely. Orientation, attention, comprehension and simple calculation were unimpaired. His general intelligence was good.

Physical status.—He was a ruddy-complexioned, fairly well-developed and well-nourished man of "athletic" type. The right pupil was slightly smaller than the left and slightly irregular. Both pupils reacted promptly to light, directly and consensually, and there was no other abnormality in the visual apparatus. A watch was heard at 18 in. with either ear. The tongue was protruded in the mid-line, with a coarse vermicular tremor. The tendon-jerks were normal. The epigastric reflexes were equal, and the abdominals absent (fat). The plantars gave an atypical extensor response, all toes extending jerkily. There was tremor of the right arm even at rest, and much increased on voluntary movement. When asked to make a movement he made it much less powerfully than when not asked to do so, e.g., the left ankle was very fully flexed when the Achilles jerk was tested, but very much less flexed when he was asked to move the ankle. All muscular movements asked for were performed with great effort and heavy breathing, and were done feebly and jerkily, with contraction of the antagonists. He touched his nose accurately with the first finger of each hand after much waving about in the air. The heel-to-knee test was accurately performed after much effort and jerking of the limb. His gait was straddling, with his back very much bent forward. The other systems were normal. The blood-pressure was 114/80 (lying). The blood Wassermann was negative. He complained of pain in the lumbar region, to which he attributed his posture, and there was diffuse tenderness on pinching lightly over a large area of his back. The hyperæsthetic area varied in extent at different examinations. No other sensory disturbance was present. X-ray revealed no disease of the lumbar spine.

Course in hospital.—Two weeks after entering the hospital, with verbal and electrical persuasion, and massage, he was walking practically erect, without a straddling gait. After four days of this he relapsed almost completely one morning following a "dream," in which he heard the words, "You will be carried out of this hospital—you'll never leave it otherwise." On waking after this dream his lumbar pain was worse and he felt depressed. He remained depressed, emotional and tremulous. His gait improved somewhat, but still he carried his trunk forward. When lying on his bed face downwards his back was well arched and he did not complain, until the arching was pointed out to him, when he groaned and bent forward. For a day at a time he would walk much more easily—"When I'm well I say so"—and he showed a kind of pseudo-elation. He said once that he was afraid to return to his work. Later he denied this remark, but it was known from other sources that he realized he was getting too old for the strenuous type of work he had been engaged in. Finally, after three months, he had to be discharged, as he showed no signs of special improvement, and although avowedly co-operative continued to emphasize his disabilities such as "defective memory," and even a fear of traffic and of the dark.

Comment.—The physical signs in this case were for the most part obviously not of organic origin—the straddling gait without reflex or

sensory alteration; the type of tremor; the weakness of commanded movements only; the peculiar diversity of the signs; their variable intensity; especially on observation, and the diffuse but variable hyperæsthesia. All these physical signs could be voluntarily imitated. The history may therefore fairly be assumed to be one of a psychogenic disability.

It accordingly becomes interesting to note:—

(1) The latent period between the trauma and the occurrence of outspoken disabilities.

(2) The emotional accompaniments of the trauma, including both fear of falling among machinery and resentment against his superior. The influence of the emotion of fear in determining later symptoms and signs is evident—weakness in the legs and general tremor being felt at the time; and being objectively perpetuated as tremor of arms and disordered gait.

(3) The underlying motive—escape from work that he felt to be getting beyond his capacity, and the obtaining of compensation.

(4) The mental attitude—the patient emphasizing his disabilities and yet protesting his desire to be rid of them. His emphasis on his mental symptom is of the same kind. There was an absence of real concern. He complained of his symptoms, but failed to inquire *how* to be rid of them.

(5) The type of mental symptom—depression, irritability, a feeling of guilt, rather unusual and not unrelated perhaps to a more or less conscious knowledge of the nature of his illness, and a selective type of memory defect, “emotional stupidity.” Also the feeling of being “insulted” is interesting, as he seemed to have lost the association with the episode of the under-manager.

(6) The suggestive effect of certain episodes prominent in his narrow life: (a) The previous accident with the suggestion that symptoms might reappear at a long interval; and (b) his father's recent death after an accident.

(7) The history itself is one that satisfies a number of the criteria for the establishment of a psychogenesis—the trauma resulting in the immediate appearance of certain phenomena directly referable to emotional disturbance; the appearance after a latent period of disabling symptoms attributed by the patient to the trauma and really the overt expression of continued rumination; and the pre-traumatic existence of a general setting of emotional unrest, especially dissatisfaction with work.

SUMMARY.

In the light of a study of the cases recorded or alluded to above, and of experience of other similar cases, it is clear that in the absence of unequivocal physical signs and of a characteristic history pointing to physical disease, the differentiation of psychogenic affections with physical symptoms from psychogenic disorders requires investigation in a number of directions, none of which in itself yields conclusive evidence. Further, unless the results of investigation agree in several of these directions in establishing a psychogenesis, there can be grave doubt as to the psychic origin of the symptoms in question. The commonest error is to mistake a psychogenic disorder for a physiogenic; but the converse is by no means rare. In the thirteen cases which prompted the writing of this paper, there had been at least nine erroneous diagnoses, of which five were of organic disease where only psychogenic symptoms were present; but in no fewer than four a diagnosis of psychogenic disorder was made when the condition was one of organic disease. There is undoubtedly a certainly facile tendency which ascribes to any obscure physical symptoms a "functional" origin, and another error creeps in when every "functional" disorder is assumed to be psychogenic. Nevertheless, this latter assumption is probably more often correct than not.

(1) The first criterion is, of course, the nature of the physical signs present, if there are any. If the physical signs are relevant to the complaints, then from the diagnostic point of view, although not from the point of view of treatment, it is not necessary to go further, except for the purpose of assessing any suspected psychogenic element in the disability produced (e.g., Case 1). But if the physical signs are not apparently relevant, or are vague or altogether wanting, then the case has to be explored along the lines already indicated in the comments on cases. In the first place, there is something to be learned from physical signs that are not characteristic of organic disease. This generalization may be made: there is a presumption of psychological (non-organic) origin for all physical signs that may be produced either by the direct effect of emotional disturbance or by the patient's volition. Examples of the first group are tremor, tachycardia and diarrhoea, and of the second group paralysis and tics. On applying this criterion to a series of cases, including the nine recorded above, it was found that in every instance the signs not definitely known on other grounds to be organic fell into one or other of these two groups. Thus, in the hysterical patients the motor signs were usually capable

of complete voluntary imitation; and where imitation would have been difficult, they were explicable as the results of emotional excitement. In Cases 5 and 8, the leading symptoms (tremor in the one case and palpitation in the other) are well known as accompaniments of fear. In Case 3 there was a combination of emotionally produced and of easily imitable phenomena—tremor and difficulty in speech and writing. In Cases 3, 4, 6 and 7, which were all basically organic in nature, much of the difficulty of diagnosis arose from the superposition of signs of emotional origin on an organic disease, since organic disorder does not confer immunity from emotional reactions.

(2) The second criterion or set of criteria which presents itself is the type of history of the illness itself. There are common types of history which are indisputably those of a physical disorder, e.g., the account of an attack of gall-stone, colic, or the history of duodenal ulcer, where the sequence of symptoms is characteristic and almost invariable. It is not in such conditions as these that doubt arises.

It is a rough but useful generalization in neurological diagnosis that sudden lesions are due to trauma or hæmorrhage, more gradually appearing lesions to inflammatory processes, and those of slowest onset to neoplasms. Something analogous exists in clinical psychiatry. Suddenly appearing signs in a previously apparently healthy person result from immediate psychic trauma; those appearing more gradually from rumination over a recent or contemporary situation, and signs and symptoms of very slow onset from the continued more or less unconscious growth of complex material over a long period of time.

Where the onset of certain signs and symptoms coincides in time with certain events, it is justifiable to suspect strongly an association between the two. Where there is a repeated coincidence of symptom and provocative situation, the suspicion is strengthened. In Case 5, where the physical signs developed suddenly and repeatedly, the psychic traumata were easily traced at each repetition, and since the physical sign (tremor) was of a type frequently expressive of emotion, the assumption of an ætiological relationship is doubly justified. Extending this method, the repeated association of a trying situation with a symptom otherwise ambiguous can be held to make the psychic origin of this symptom extremely probable. In Case 9, where there was an interval between the trauma and the appearance of disablement, it is inviting to fill in the gap. This was partly possible on discovering that vengeful rumination followed the trauma, and that pessimistic reflection on his working capacity and his age had existed for some time.

(3) A general setting of psychic disequilibrium is necessary for the development of a psychogenic disorder in response to external factors. A psychic trauma falling upon a healthy mind usually produces no prolonged after-effects; but in a discontented, fearful, depressed or sensitive person, it is very apt to precipitate an outbreak of symptoms. In all of the patients under consideration in whom the illness was purely psychogenic, such a general setting could be demonstrated. In Case 3 the continued sweeping affective change, upon which as a background the other functional symptoms transitorily appeared, was obvious. In Case 8 there was dislike of his occupation, as a leading trend among a number of causes of unrest (feeling of educational inferiority, and masturbation). The position was similar in the other patients in whom were found such factors as loathing for work, long-standing feeling of inferiority, and apprehension of incapacity for work with advancing years, from which the trauma provided a welcome escape (Case 9); in another case, trying conditions of long standing (long hours of business, chronic illness of parents, and brother's defaults), all the more potent because the patient had refused to recognize them; and in another where there had been almost lifelong dissatisfaction with her position of drudge to her father and a half-overt rebellion against him.

It seems therefore permissible to state that a canon that should ordinarily be satisfied before the psychic origin of a physical sign or somatically-expressed symptom is established, is that a general setting of psychic dissatisfaction should have existed before the appearance of the sign or symptom.

The possible exception seems to occur in those circumstances where the occurrence of a trauma itself produces a craving for something not hitherto aspired to and, therefore, furnishes an opportunity for dissatisfaction, e.g., the possibility of compensation for a railway accident.

(4) A topic of investigation closely related to the last is that of the personality or "make-up" of the patient. In Case 5 there was a customary attitude of timidity to life in general. In one patient, in whom the origin lay in a distant past in childhood which the patient could not recall to furnish clues, it was clear that the patient was of an unusual type—narrow and undeveloped in her interests, shy, sensitive and antagonistic, and her illness could be regarded as something that had unfolded itself as her personality developed and had been woven into it. In most of the other purely psycho-neurotic states under discussion

similar but not such disadvantageous deviations from the normal were demonstrable. The only exception was Case 9, where it was not possible to get the patient's full co-operation, or that of his friends, in an inquiry into his previous make-up. It is certainly justifiable to regard aberration from the average types of personality as weighing the balance in favour of the psychic origin of an illness.

(5) In practice the mental attitude of the patient to his signs and symptoms is the criterion on which perhaps most stress is laid in the clinical summing-up of doubtful cases. There is something indefinable in the attitude of the neurotic that is different from the attitude of the normal person. From the cases under review, we might attempt to define the attitude as consisting either in an excess or defect of concern, together with (in both extremes) a lack of persistence and determination in carrying out therapeutic recommendations. Either the patient is too anxious about his trouble (Cases 5 and 8), or he is not anxious enough (Case 9). In the first instances the troubles overwhelm him and disorganize attempts at remedy, while in the second he is not only lazy but may even be antagonistic to treatment.

(6) Finally, the physician should apply the criterion, which is an invaluable one in the study of psychogenic illness, namely, the purpose which the latter seems to fulfil. The purpose may, of course, be a very subtle one, or it may be the securing of a definite material gain (Case 9). Where there seems to be nothing but disadvantage accruing, and when there is little discoverable cause for dissatisfaction, as in Case 2, the psychic origin of symptoms must be doubtful. But even where a definite advantage seems to be gained, this may be an accident (Case 1).

[This work was done as Henderson Research Scholar, Glasgow, 1925.]

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NOTICES OF RECENT PUBLICATIONS.

The Basis of Sensation (The Action of the Sense Organs). By E. D. ADRIAN. Pp. 122. London: Christophers. 1928. Price 7s. 6d.

The first conclusion arrived at in this extremely interesting book is that the impulses set up in sensory fibres by appropriate stimulation of their end-organs are essentially the same as the impulses that have hitherto been studied almost exclusively in motor nerve-fibres. The author's investigations have been carried out with a capillary electrometer used in conjunction with a four- or five-valve amplifier such as is employed in wireless work, and by this means he was able to study the nature of the message transmitted to the central nervous system when a nerve or its end-organ is stimulated. He has found that in the sensory nerves, too, each impulse is followed by a very brief refractory period, so that the message consists of a series of discrete impulses, never in continuous transmission, and that the only way in which it can be made to vary is by a variation in the total number of impulses and in their frequency.

It has been possible to study the action current of single nerve-fibres, and even, by an ingenious method, the effect of stimulating a single sensory nerve-organ in a muscle; in this instance it was found that the impulses have a frequency of about thirty per second, and that the frequency varies with the strength of the stimulus and declines on prolonged stimulation. The intensity of the sensation evoked seems to be directly proportional to the frequency of the impulses in the nerve. Physiological stimulation of other end-organs by pressure and touch, and by painful and postural stimuli, has shown that there are no radical differences between the impulses that produce various modes of sensation, but there is evidence that a discharge must have a certain mass to excite pain, so that while a brief discharge in certain nerve-fibres gives rise to a sensation of contact, a persistent discharge in the same fibres may evoke pain. The quality of the sensation seems to depend, therefore, on the paths which the impulses take. Although the author avoids scrupulously any attempt to explain what occurs in the higher levels of the nervous system, he points out that the mental correlate must be a very close copy of the physical events in the peripheral nerves.

In this work Dr. Adrian has opened up a new field of investigation that must in time have an important influence on clinical and psychological work.

The Examination of the Nervous Systems. By DONALD CORE. Pp. 248. Edinburgh: E. and S. Livingstone. 1927. Price 8s. 6d.

Textbooks on the methods of examination of the nervous system are naturally intended for the use of students and those with a special interest in neurology,

and consequently they must, to be of use, fulfil certain requirements. In the first place, they must be systematic and as concise as is practicable with clear exposition; in the second place, the methods of investigation advised should be described accurately and in sufficient detail to make them easy to apply, and finally, the student should be instructed where possible in the physiological as well as the pathological significance of the results elicited by his tests, for only then can he acquire an intelligent interest in the subject.

This book will undoubtedly impart much useful information to the medical student for whom it is written, but it would have served its purpose more efficiently if its arrangement had been more systematic and the descriptions more detailed and in places more concise. In the first chapter the student is introduced, under the heading "motor system," straight away to tremors and other involuntary movements before he has learned anything of the tone or power of the muscles or of the co-ordination of movement, all of which are concerned in them. A few short paragraphs here on the special features of motor paresis due to different organic affections and its distinction from psychogenic feebleness and feigned loss of power, would have been useful and enlightening. The section on inco-ordination would stand expansion, and the descriptions of certain tests, as adiadochokinesis, labyrinthine investigations and others, are incomplete for even ordinary routine work. Diplopia is referred to, but the rules by which the ocular muscles affected may be identified are almost neglected, and apraxia is not mentioned, though the condition to which the term is given is referred to in a short paragraph on psychomotor disorders. The chapter on the mental state of the patient is fuller and more satisfactory. The book can be improved by compression of some sections, and greater detail in others, in its next edition.

The Clinical Examination of the Nervous Systems. By G. H. MONRAD-KROHN. Pp. 209. London: H. K. Lewis. 1928. Price 7s. 6d.

There is little change in the new edition of this book which has already proved so useful to students of neurology, but it is regrettable that the short chapter on the interpretation of radiograms of the skull that has been added neglects some important points, and has not dealt with the essentials at least of pneumoencephalography.

Epilepsy: Comparative Pathogenesis, Symptoms and Treatment. By L. J. J. MUSKENS. Pp. 435. London: Baillière, Tindall and Cox. 1928. Price 27s. 6d.

The original German edition of this book has been already noticed in this Journal (vol. xlix, p. 434). There is little change in its English translation, which is readable and well reproduced, but on a few points the author has taken the opportunity of revising his text and bringing it up to date.

An Introduction to Forensic Psychiatry in the Criminal Courts. By W. N. EAST. Pp. 381. London: J. and A. Churchill. 1927. Price 16s.

This book fills a gap in English psychiatric literature, as till it appeared we had no medical treatise devoted wholly to the legal aspects of unsoundness of mind, a subject which, with the coming into force of the Mental Deficiency Act, has become more important to every physician who may be brought into professional contact with persons charged with criminal offences.

The qualifications of the author for the task are undoubted, as he has spent the greater part of his professional life as a prison medical officer in intimate contact with criminals, and in frequent association with the Courts of Law. His book is characterized by common sense and level judgment, and every aspect of the subject is illustrated by cases which came under his own observation, or which he has taken from legal records.

After preliminary chapters on "ascertainment," or the methods of examination of the mental state of an accused person, and on "practice and procedure," which deal mainly with the legal aspects of the case, the thorny question of criminal responsibility in English law is fully considered, with perhaps more emphasis on its legal than its psychological side. Then each form of mental deficiency and disease, including hysteria, is considered separately, and the tendency in each to anti-social acts, the forms these may take, as well as the special problems each presents to the medical witness in the Courts of Law, are adequately considered.

Vagotonies, Sympathicotones, Neurotonies. Les états de déséquilibre du Système nerveux organovégétatif. Par A. G. GUILLAUME. 2me Edition. Pp. 562. Paris: Masson et Cie. Prix 40 francs.

The second edition of this book is more than double the size in which it originally appeared. Most of the chapters have been rewritten or remodelled, and several new ones have been inserted, as one on the relation of the sympathetic system to the blood, and another on its influence on the mind. Its aim is an ætiological and clinical study of disturbances of balance of the autonomic nervous system, especially as seen in the so-called states of vagotony, sympathicotony and neurotony, but the author has cast his net so wide, and has included so many conditions that even his persuasive arguments can scarcely relate to the vegetative nervous system, that the reader finally becomes a victim of confusion and scepticism, for even the clinical aspects of the best recognized of these conditions are vague and indefinite, and of their pathology we know little or nothing.

That the visceral organs in disease may through their nerves exert a considerable influence on the mind, and especially on its emotional side, is generally admitted, but to attempt, as the author does, to bring hysteria, neurasthenia, and other psychoneuroses into the realm of sympathetic pathology, seems in

the present state of our knowledge unjustifiable. The book carries the impress of the author's enthusiasm and learning, and contains a valuable epitome of most of the work that has been done on this neglected subject, but too free quotations from others who support his views make its reading wearisome.

The Development of the Human Eye. By IDA C. MANN. Pp. 306. Cambridge University Press, for the *British Journal of Ophthalmology*. 1928. Price 36s.

The publication of this work on the development of the eye has done good service to a branch of scientific study in which embryologists, anatomists and zoologists are, at least, as much interested as ophthalmologists. During the last ten years Miss Mann has published in different journals a series of papers dealing with various aspects of the development of the human eye; the publication of this book gives us the opportunity of appreciating more easily the value of the great amount of work which she has done on a subject in which she has become a recognized master. Much of the subject-matter is based on her own investigation, and throughout it she has refused to accept the conclusions of others without verifying them. Most of the illustrations are from her own drawings of actual specimens, and mainly from human embryos in the fine series which Professor Frazer has gathered together. Many obscure problems in the embryology of the eye remain to be solved, but all future workers owe a debt of gratitude to the author for her lucid exposition of the present state of knowledge.

Die Behandlung der Giftsuchten. Alkoholismus. Morphinismus. Kokainismus. By VON ERNST JOEL. S. 118. Leipzig: Georg Thieme. 1928. Price M. 5.

This is an admirable presentation of the methods by which drug addiction should be treated. The author has had unusually wide experience of the problem in all its bearings, and his consideration of the social and psychological factors, as well as the pharmacological, is not merely a rehash of familiar views. In the introductory "General Considerations" he draws a helpful distinction between somatic and psychic habituation, and points out the influence of mental conflicts, especially in the sexual domain, and of economic conditions.

His advice as to treatment of alcoholism, as in the other parts of the book, is sound, explicit and detailed, and does not neglect the important question of after-treatment. With regard to morphinism, the author emphasizes that after a time the habitué no longer gets any pleasure from the drug, but has to take it to alleviate the physical symptoms of deprivation. Many of the minor practical points that crop up during the treatment are gone into, and the much debated question of abrupt or gradual withdrawal of the drug is regarded as one to be settled separately in each case. The section dealing with cocaineism is

brief and interesting. Caffein, veronal, ether and tobacco addictions are also discussed, a distinction being made between nicotism and the misuse of tobacco. The legal aspects of addiction and the various channels through which addicts obtain their drug are set forth.

The therapeutic manuals, of which this is one, are intended to present "the scientific foundations of treatment and their practical application"; this book is a model in that respect.

Psychopathology: Its Development and its Place in Medicine. By BARNARD HART. Pp. 156. Cambridge University Press. 1927. Price 7s. 6d.

After a brief historical summary, the author examines critically the chief conceptions of psychopathology obtaining at present, the tenets of the Freudian school receiving particular attention. In a field where one usually finds much heat and dust and little light, it is pleasant to meet with so balanced and lucid an attempt at just appraisal, without acrimony or fervour. The merits of Janet are recognized, but the greater value of a dynamic interpretation is set forth. This leads to a consideration of Freudian theories; the psycho-analytic method, as a weapon of scientific investigation, is weighed and found wanting, but Dr. Hart concludes: "Although the theories of Freud do not attain the standard demanded by the canons of science, some of his conceptions approximate very nearly to that standard, and perhaps as nearly as any psychological conception can approach." There is an appendix on the conception of the subconscious, co-conscious and unconscious.

The war-time essay on "The Psychology of Rumour," which is included, is an interesting example of the application of the psychological method to the study of social phenomena; the psychology of evidence is brought into relation with the problems of crowd-behaviour and the influences of complexes in accounting for the spread of rumours and for their content.

There is a final essay on "The Methods of Psychotherapy," which are considered as dependent on the use of three basic principles, affective therapeutics or suggestion, persuasion, and analysis. The essay illustrates the clarity of thought which Dr. Hart evidently pleads for. This book will be illuminating to physicians generally, and not only psychiatrists who practise psychotherapy.

Les Obsédés. Par RAYMOND MALLET. Pp. 116. Paris: G. Doin et Cie. 1928. Price 12 francs.

This book is essentially clinical; the first quarter is given to case records, with brief comments, and most of what remains to a description of the symptoms, clinical forms and course of the disorder. But, on the other hand, the term "obsédé" is given a wide application, so as to cover anxiety, physical disorders, ideas of influence and depersonalization; the diagnosis is not always unexceptionable, and one could regard some of the illustrative cases as examples of quite a different reaction-type. There is, moreover, an occasional vagueness

and looseness; thus, we are told that the often found visceroptosis, hæmorrhoids and hernias are evidence of "a congenital dystrophy of the elastic tissue," and that it is interesting to bring this "hypotonicity, this physical plasticity, into relation with the patient's mental plasticity"; while neurasthenia may be a "congenital feebleness of nervous resistance (constitutional neurasthenia), resistance to fatigue in general, not to emotions in particular." These conditions are regarded as due to a defect of "organo-psychic synthesis." The part played by psychic automatism is considered as fully as one would expect in view of the importance ascribed to the mechanism in recent French psychiatry.

The author deprecates analysis or hypnotism in treatment, and relies on rest, reassurance, suggestion and drugs. For those who wish to acquaint themselves with current French views on diagnosis and pathogenesis, the work will be interesting.

The Measurement of Mental Capacities. A Review of the Psychology of Individual Difference. By CYRIL BURT. Pp. 52. Edinburgh and London: Oliver and Boyd. 1927. Price 6d.

This, the seventh of the Henderson Trust Lectures, serves to remind us, as did some of its predecessors, that there was much besides dross in the "pseudo-sciences," phrenology, physiognomy, graphology and cranioscopy, on which Oliver Wendell Holmes poured so much ridicule.

Professor Burt points out how the method of correlation has been extended to psychological inquiries; and after a brief discussion of the value of physical criteria in mental measurement, he passes on to consider the correlates used in the application of mental tests in the stricter sense. There is then an enumeration, necessarily tentative, of special capacities or "group-factors," and the difficulties in the way of analysing character are mentioned. The lecture ends with a review of the increasing importance of these studies and the need for further research.

There are a few controversial statements, e.g., the allusion to obsessions in connection with the group-factor, perseverance; and one wished that Professor Burt were not so fond of Jung's unfortunate division of people into extraverts and introverts, but to discuss these matters would be beside the point. Mental testing is applied in so many circumstances that a knowledge of its principles is very desirable, and this is a clear and authoritative presentation of them.

Mental Disorders. A Handbook for Students and Practitioners. By HUBERT J. NORMAN. Pp. 463. Edinburgh: E. and S. Livingstone. 1928. Price 14s.

This elementary handbook is intended mainly for the junior student, but even from this standpoint it can scarcely escape criticism. That "much of modern psychiatry is still in an inchoate condition" is not an adequate excuse

for the failure to discuss modern tendencies, and apart from theories there is a general neglect of current conceptions; for example, it is not pointed out that the Korsakow type is common to all the organic psychosis. The section on treatment reflects the author's practical experience, but it is a pity that so much more stress is laid on drugs and seclusion than on psychotherapy and on hydrotherapy, the great value of which is scarcely recognized. The account of literary and historical persons who suffered with mental disorders is superficial and neglects the large literature, especially in French and German, on the subject.

Studies in Psychology. By WILLIAM ELDER. Pp. 212. London: William Heinemann. 1927. Price 8s. 6d.

The author's main object is to relate mental phenomena to changes in the vital neuron mechanisms. A large part of the book is devoted to the study of memory and sleep, with particular attention to dreams. It would be impossible for these matters to be discussed without frequent reference to Freud; Dr. Elder goes roundly to work with him, and there is none of that coquetting with the new doctrine that is often evident among its professed opponents; he denies the unconscious in good set terms. Sleep he regards as instinctive; "by oft repetition it has become in most people a habit." Dreaming is "parti-conscious thinking."

There are also chapters on emotion, will, consciousness and dissociated states. The author adheres to the association-psychology, with leanings towards behaviourism, where he is not approaching the subject from the neurological side. He has made an obviously sincere effort to correlate the available data, but his bias is too strong.

Les syndromes mentaux. Par A. PAROT. Premier fascicule. Pp. 370. Paris: Gaston Doin et Cie. Price 55 fr.

The present work is an excellent clinical account of the forms in which the syndrome "mental confusion" may be met with. A detailed description of its psychic and physical characters is contained in the first part of the book; and the succeeding chapters cover the syndromes of toxic, traumatic, endocrine and autonomic; metabolic, encephalopathic and emotional origin. Emphasis is laid on the forms which the confusional syndrome may assume and the clinical course it may follow. There are disadvantages in this method of presentation; for example, the main clinical picture of mental disorder associated with organic disease of the brain, such as general paralysis and arterio-sclerosis, is not considered along with the toxic psychoses or the other encephalopathies but with the dementias; and the conception of the confusional syndrome is so wide that it cuts across all the usual categories, but this is evidence of an important tendency in recent psychiatry. The book is free from German or other foreign influences, and it is perhaps fortunate that there should be available so unadulterated a presentation of French psychiatry, in

which we can read of psycho-sensorial erethism, of mental automatism, of the influence of hepatic insufficiency or of the vegetative nervous system, and other unfamiliar things, and from which we may see how active and valuable is the work of this school.

Neurologische Wandtafeln. Herausgegeben von F. MÜLLER, F. HILLER und H. SPATZ. 2te Lieferung. München: J. F. Lehmann. 1928. Price 100 marks.

Two years ago the first series of these anatomical charts appeared. The second series includes ten new charts, which are designed with equal care and published in the same clear and artistic form. The first gives a diagrammatic representation of the pyramidal tracts and of the chief sensory paths in distinctive colours; in the next the sensory root areas on the surface of the body are shown. The superficial areas of sensory peripheral nerves, the motor points of the chief muscles, the relations of the motor nerves to the spinal segments, and of the spinal roots to the vertebral spines are represented in two other charts. The main features in the development of the brain are represented in a chart in which the close relation of the corpus striatum to the cortex is distinctly shown, and in another, stages in the myelinization of the brain and spinal cord are figured. There are also excellent diagrams of the structure of some of the chief areas of the cerebral cortex, as visible in Nissl and Weigert preparations, and of the innervation of the thoracic and abdominal organs by the sympathetic and parasympathetic systems. Two charts, however, scarcely attain the excellent level of those of the first series or the other of this; in the diagram of the visual paths the relations of the optic radiations, especially in the region of the internal capsule, and the projection of the different portions of the visual fields on the calcarine cortex, might have been shown in greater detail, and it is a pity that in the chart of the blood-supply of the brain the arteries of the surface only are represented. This second series of charts will be as indispensable as the first for teachers of clinical neurology and of the anatomy of the nervous system.

Funktionen des Zentralnervensystems (Teil 5B, Heft 5, des *Handbuches der biologischen Arbeitsmethoden*, herausgegeben von A. ABDERHALDEN). (1) *Neurobiologische Studien am menschlichen Fœtus*, von M. MINKOWSKI. (2) *Methoden der Reflexprüfung beim Menschen*, von A. BÖHME. S. 182. Berlin und Wien: Urban und Schwarzenberg. 1928. Price 10 marks.

Although the aim of Abderhalden's Handbook of Biological Methods which is now appearing, is to give descriptive accounts of all methods of biological investigation, both these articles are written from a wider and less technical point of view.

Minkowski summarizes his earlier papers on the physiological investigation

of the human foetus and describes his methods. His material consisted of embryos and fetuses removed by a modified Cæsarean section on urgent medical grounds. The foetus, especially when extracted under local anæsthesia and placed immediately in a saline solution at body temperature, continued to show various movements and reactions to external stimuli for a considerable time, and as the specimens were not viable it was possible to investigate the nature and the levels of these reactions by destruction of different parts of the nervous system. Some movements may be observed from the second month of intra-uterine life, but these are probably idiomuscular and independent of the nervous system. In the third and fourth months these gradually give place to true reflex reactions, which under the influence of the developing nervous system become progressively more localized, more specific and more purposive. The nature of all these reflexes is analysed in detail, and their bearing on clinical as well as on the physiological phenomena of adult life is emphasized. Minkowski's work therefore enables us to go a step further back in interpreting the significance of disturbances of function in the light of their normal evolution.

Böhme gives a full description of the various reflexes that can be elicited in man under normal and pathological conditions, including the postural and labyrinthine reactions. He discusses concisely, and with reference to the latest physiological work, the different varieties of reflexes he describes. These two articles should prove of the greatest assistance to the clinical neurologist.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BAILE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

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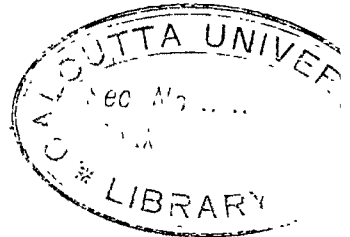
To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

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OCULOGYRIC CRISES IN CHRONIC EPIDEMIC ENCEPHALITIS.

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INTRODUCTION.

CHRONIC epidemic encephalitis has from the first been associated with manifestations of a bizarre and striking character. The majority of these phenomena have been of a hyperkinetic type and include choreic, athetoid and myoclonic movements, motor tics of all descriptions, generalized convulsions, paradoxical activity, respiratory crises, and lastly, the tonic eye spasms termed by the French *crises oculogyres*. These have been recognized for little more than three years, and it is doubtful if they occurred before 1923.

There can be little doubt that certain of these hyperkinetic manifestations, such as the myoclonic and respiratory phenomena, are on the wane, and none at all that the incidence of oculogyric crises is increasing. Our series of 23 cases is taken from a total number of 136 encephalitics, all of whom are, or have been, patients in West Park Mental Hospital or the Manor Institution for mental defectives. This constitutes an approximate proportion of 17 per cent. It is a matter of some difficulty to obtain accurate histories of the onset of the attacks in all cases, but as far as can be ascertained in only 6 of the 23 cases did the crises occur before 1926. On the other hand, 5 out of the last 9 encephalitics admitted to West Park have been thus affected. The earliest date of origin in our series appears to be 1923; another case started fairly definitely in the autumn of 1924. There is evidently no relation

between oculogyric crises and any special epidemic, as the dates of the primary attacks of encephalitis that were followed by crises include every year from 1919 to 1925. Again, it is impossible to foretell how long after the primary illness the onset of this phenomenon may be expected, as in two of our cases the attacks commenced within six months, while several remained free for six years, and in one there is no evidence of the crises beginning until eight years after she first became ill. In all our cases the onset of Parkinsonism preceded that of the crises, but periods varying from a month or two to five or six years separated the onset of the two syndromes. The nature of the primary attack likewise offers no criterion as to the possibility of the development of ocular spasms, and our series includes all varieties of primary illness, acute and gradual, mild and severe. This lack of relationship helps us little in forming an hypothesis of the origin of these attacks, except that it tends to emphasize the progressive nature of the disease and the unimportance of the nature of the primary attack and of the epidemic on the resulting sequelæ. The increasing prevalence of this distressing manifestation is another problem that at present must be left unsolved.

No theory appears to us sufficiently reasonable to put forward, and we can but wait for fresh light to be thrown upon the subject by means of larger experience and further investigations. The suggestions as to the pathological basis of these manifestations which we are bringing forward in this paper are evolved from clinical considerations, combined with certain facts in the physiological anatomy of the ocular mechanisms. These support our view that the lesion accountable for the crises does not lie in the lower centres for conjugate deviation, but in the associational centres or paths leading to them.

The mental state of these cases, especially in association with their attacks, is compatible with our theory that there is a diminution of normal cortical inhibition which allows of the occurrence of the attacks, and that the crises are comparable with other phenomena of a "release" nature.

CLINICAL MANIFESTATIONS.

Type of Case in which found.

In a previous paper [4] we made a classification of the mental types of chronic epidemic encephalitis into bradyphrenic, depressed, paranoid and behaviouristic, with certain subgroups. The usually accepted classification from a neurological approach is into extrapyramidal or Parkinsonian, pyramidal and intermediate types [15]. We can state

that oculogyric crises may appear in any of the various mental types, and further, that they show no special predilection for any of them. From the neurological side all our cases have been associated with Parkinsonism and have been fairly equally distributed amongst all degrees of this syndrome. One might have expected to find oculogyric crises more common amongst patients who showed other ocular abnormalities, a bare enumeration of which would merely be a list of practically all the signs and symptoms possible from lesions of the ocular nervous apparatus. As a matter of fact, experience does not bear out this expectation, and some of our cases with oculogyric crises are singularly free from other elements of the encephalitic ocular syndrome. This fact may be correlated with the pathogenesis of these crises, which tends to show that they are due to lesions affecting the cortical inhibitory paths and those to the ocular supranuclear centres, which means that the causal lesions may well be quite distant from the central ocular nervous apparatus itself.

It is, of course, impossible to be dogmatic on 23 cases, but certainly our experience tends to show that age and sex are quite unimportant. Fourteen of our cases are males with ages ranging from 15 to 42, while the nine females also vary from 15 to 42 years. The majority are certainly males and under 25, but this is roughly proportionate to our total cases who number 136, of whom 87 are males, and of these 63 are under 25. We consider the high proportion of our cases exhibiting these crises to be due to two causes; the first, and in our opinion much the less important, is that owing to continuous observation in a hospital the attacks are not likely to be missed when they do occur. That they are overlooked in many cases is certain, for quite a few of our patients suffered with them for long periods prior to admission, without any attention having been paid to them. The second and more important cause is that the crises are in part dependent on an interference with cortical inhibitions, the lack of which is also the cause of many of the psychotic symptoms which lead to certification.

Associated phenomena.—Oculogyric crises may occur as isolated phenomena, or may be part of a more widespread tonic seizure. In only three of our cases is the latter condition marked, and in these the accompanying spasms are confined to the head and neck. In one (Case 1) the head is turned with the eyes to the left and is somewhat retracted (see figs. 1 and 2); in another (Case 2) the head is curved backwards, while in a third the rigidity is particularly noticeable when the deviation of the eyes and head is in a downward direction. Other

observers are struck by the relatively common coincidence of associated tonic phenomena. Thus, Wimmer [16] and Marinesco and Radovici [5] found associated tonic spasms in a large percentage of their

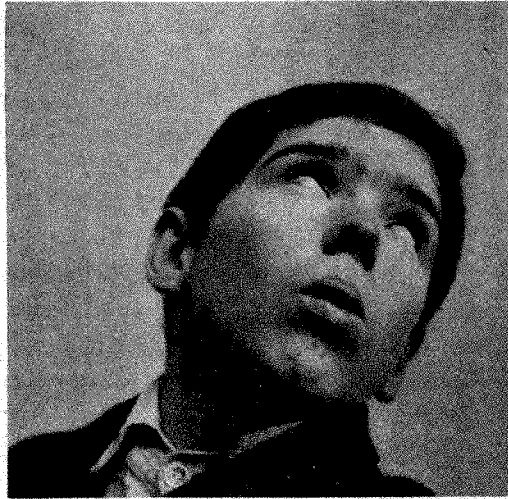


FIG. 1.—Case 1. Oculogyric crisis showing deviation of head and eyes upwards and to the left.

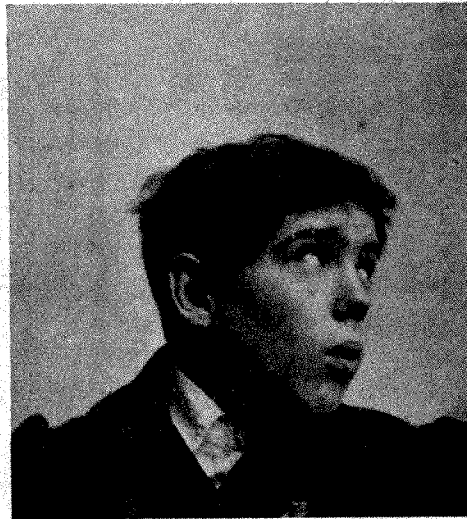


FIG. 2.—Case 1. Oculogyric crisis, showing deviation of eyes up and to the left with slight turning of head to left.

cases. In all such cases it is apparent that the stimulus first attacks one of the centres of conjugate deviation and, if strong enough, overflows into associated centres to cause co-ordinated movements normally

associated with the deviation, the head always turning in the same direction as the eyes and, when torsion of the trunk and limbs have been recorded, this also has been in the direction in which the eyes are fixed. In the majority of cases a feeling of helplessness is experienced, and this is sometimes accompanied by a feeling of inability to speak, but in no case is either of these symptoms absolute. Inability to close the eyes is fairly common. The crises are accompanied almost invariably by feelings of mental discomfort, often amounting to definite distress, but physical pain is unusual. Slight headache or more commonly aching of the eyeballs, is complained of, but is of obviously minor importance to the patients. The feeling of distress appears to be a phenomenon akin to the sensation of impending dissolution experienced in angina pectoris, and in a lesser degree in some vaso-vagal attacks, one patient actually volunteering that she feels she is going to die during the crises. Another interprets it as a fear that her eyes will remain up for ever, while a patient recently admitted describes feeling as if his eyes were going right up and that he was going blind. These ideas recur during every crisis, and are doubtless similar to what Stern [11] describes as compulsive thoughts associated with tonic eye spasms. In several of our cases the crisis is accompanied by screaming or crying; in one stamping of the feet and general excitement is a usual concomitant, whilst another provides an exhibition of violence and obscene language of unusual degree, which lasts for hours after the oculogyric crisis has terminated.

These exhibitions of abnormal behaviour are such as are usually regarded as due to release from cortical inhibition, a phenomenon which we consider of great importance in these crises. Fatigue and emotion are common antecedents of individual attacks, and both are well recognized as paralyzers of voluntary control, even in the healthy subject, so that it is not surprising that they are potent factors in our patients. There is abundant clinical evidence to support the thesis that lack of cortical inhibition is an important mechanism in the mental symptoms seen in encephalitics. It explains the characteristic temperament, with its childish exhibitions of temper and impulsive unthinking acts, apachism being the example *par excellence* of uninhibited behaviour. All our patients, therefore, show evidence of a general disturbance of cortical inhibition, and the majority show it in a special manner in association with their crises. This is clearly seen in certain cases where the peculiarly close association between the ocular and emotional disturbances points to some common factor bringing them more or less

simultaneously into play. We refer to the cases where maniacal outbursts immediately precede or occur at the same time as the crises, and may last for longer or shorter periods than them. In some of these patients one or other of these phenomena may occasionally occur alone, showing that they are not altogether parts of one and the same condition, and when this does occur the patient will sometimes volunteer the statement that he was surprised that either the crisis or the mental outburst had occurred alone. This association is particularly striking in five of our cases, who are simple well-behaved bradyphrenics, apart from the outbursts associated with their crises. Several of our patients were certified solely on account of periodic outbursts of uncontrollable screaming occurring at frequent intervals. In some the ocular disturbances were overlooked owing to the overshadowing mental accompaniments, and it may be that the apparently causeless outbursts of excitement and grief not uncommonly seen in encephalitics, are more often accompanied by ocular crises than is generally suspected. The importance of recognizing the association lies in the fact that whereas ordinary apachism is unaffected by hyoscine, these outbursts accompanying oculogyric crises are usually well controlled by this drug.

Position of eyes during attack.—A typical crisis occurs rather suddenly, and the eyes may become fixed in any position. Most commonly they are turned either straight up, or upwards and to either side, the downward position being much rarer (see figs. 3 and 4). Frequently the deviation is such that scarcely anything but sclerotic is visible. One case occasionally shows fixation of her eyes in a position of extreme convergence. Sometimes there may be little or no deviation, so that the attacks manifest themselves by a fixed stare to the front or slightly to one side. These attacks easily pass unobserved, and are probably commoner than is generally supposed. That these "staring" phenomena are of an allied nature to the others there is no doubt, the accompaniments being similar and the phenomena interchangeable, not only in the same patient but even during the same attack. This we consider important in locating the site of the lesion.

Of our patients eight complain of diplopia during their attacks, and one invariably asks if she looks cross-eyed. In several of our cases the eyes are carried horizontally to one side, and in two the movement is occasionally downwards and to the left. One of these is considerably more distressed by this downward deviation than by his ordinary crises, and likes his head, which on these occasions is flexed on his chest, to be pushed up. This usually results in a deviation of his eyes into the



FIG. 3.—Case 1. Oculogyric crisis, showing movement of head and eyes downwards and to the left. (The eyelids are lifted in order to show position of eyeballs.)



FIG. 4.—Case 1. General attitude in downward crisis.

more usual position of up and to the left, a position which he prefers. There is considerable rigidity of the neck muscles and resistance against extension, but when once the eyes have adopted the upward direction the head also becomes fixed in that position. This case is very definitely against Fischer's contention that the peculiar position of the neck is a deliberate posture taken up by the patient to avoid painful cramp in the eye muscles. In many of the cases the direction of the crises is not invariable. Thus, in two patients the direction is usually up and to the left, but may be down and to the left; in Case 2 the eyes may move straight up, up and to the right, or up and to the left; in another patient they generally deviate straight up, but sometimes up and to the right; in another the movement may be straight up, up and to either side, or staring attacks may occur; whilst in one patient deviation up and to the left is commonest, but the eyes may assume any direction except below the horizontal plane. On the other hand, in three cases the position is always up and to the left, while in two it is always straight up. In one patient the attacks start by a deviation to the right, which soon gives place to a purely vertical position.

Duration of attack.—The eyes may remain fixed from a few seconds up to several hours. Case 2 has been observed in a crisis lasting a whole day with only very short intermissions, and in Case 1 an attack has frequently lasted from a few minutes after waking to 6 p.m. In nearly all cases, however, the patient is able by a strong voluntary effort to bring back his eyes momentarily to a normal position and to follow a moving object to some extent.

Time of onset of attacks.—It is notable that a fairly large proportion of attacks occur in the afternoon or evening, a fact which tends to support the well-recognized view that fatigue is an important factor in their appearance. Psychological factors are equally important, and the crises are sometimes definitely reactive to psychic stimuli. In this respect they appear to occupy a mid-place between epileptic attacks which are but infrequently reactive, and such phenomena as narcolepsy and cataplexy, in which an emotional stimulus is a usual precedent. The majority of patients show to some degree a specific predilection for certain times of the day. Two cases often have them between 5 and 6 p.m., another just before going to bed at 8.30 p.m., Case 2 between 6 and 8 p.m., while Case 1, when kept off hyoscine for a week, had continuous crises from a few minutes after waking until about 6 p.m. For the rest of the evening he was quite free from attacks. Crises are not infrequently noticed at meal times, and the reason for this may be

threefold: (i) that meals in an institution are one of the excitements of the day; (ii) that this is an opportunity for the patients to show off their accomplishments and incidentally, perhaps, to be fed by a nurse owing to their consequent inability to feed themselves; (iii) that slight attacks are less likely to pass unnoticed at this time. Several patients have regular crises just before their hyoscine injections, which may be due to a combination of two factors: (a) the wearing off of the effects of the previous injection, and (b), the excitement produced by the expectation of another injection.

Precipitating cause of individual attacks.—In the majority of crises noted by us there has been no obvious precipitating cause. Exceptions to this are not uncommon, and the following incidents have been active in bringing on attacks at various times: Interrogation and expression of interest in them, or the suggestion furnished by the sight of others in attacks; excitement, temper or grief, denoting an emotional factor; general fatigue following hard work, eye fatigue following the fixation of a near object, for some time, pointing to physical or proprioceptive stimuli; and lastly, revolving during a waltz, indicating a vestibular mechanism.

Precipitating cause of initial crises.—This subject is dealt with under pathogenesis, and here we would only state that in our opinion psychogenic factors are of very minor importance in originating the phenomena under discussion, which must be regarded as due to definite lesions of the ocular nervous apparatus. In only four of our series was a history of the circumstances of the first attack forthcoming, and in none were we satisfied that a psychogenic origin could be definitely established.

Ability to abort and prevent attacks.—Apart from the ability to stop the attack momentarily by a strong voluntary effort, most of the patients are able to influence it by other means. Closure of the eyes, whether performed actively or passively, effects a temporary remission of the crisis, but on opening the eyes again the deviation and fixation may immediately re-occur. Occasionally closure of the eyes is successful in cutting short an attack altogether, especially in less severe cases; on the other hand, many of the patients are quite unable to keep the eyes closed during an attack, and some of these continue blinking violently in an endeavour to overcome the spasm. In Case 2 this blinking has recently become so persistent that the fixation of the eyes is completely overshadowed, and she wanders about the ward with an anxious expression, blinking rapidly in what is often a vain

attempt to prevent her eyes going up. Some patients lie down and cover their heads with a rug or blanket in order to facilitate closing of the eyes. The recumbent posture has been said to relieve or even cut short the attacks in some patients, but we have only met with one case in whom lying down alone, without closure of the eyes, had any beneficial effect. Apart from these methods of influencing the attacks, which are common to nearly all the cases, many individual experiments have been tried with varying results. There is no doubt that suggestive means are at times successful in cutting short attacks; in our series, injections of water, inhalation of amyl nitrite, threats of not being allowed week-end leave, or of being stopped going to a dance, and in one case the threat of having cold water thrown over him, have all at times brought about the cessation of an attack. In others such methods have been singularly unsuccessful. Thus, one patient, who had frequent slight attacks from the time of admission, was soon sent to the ward in which the majority of the encephalitics were. Here he could see for himself the benefit of injections, and soon began to beg that he might have them. He was encouraged to believe that an injection would put a stop to his crises, and after some days an injection of water was given. To his genuine surprise and disappointment it had no effect. Later hyoscine $\frac{1}{100}$ gr. was given orally, and this effected the inhibition of attacks for thirty hours, and also brought about considerable improvement in his speech and general activity. Two or three days later a dose of aqua chloroformi made up to taste like the hyoscine mixture was given, and though the patient was told that this was exactly the same medicine as his previous dose, he stoutly maintained that it was no good. Belladonna was then tried over a period of a week, but, compared with hyoscine, the effect was very slight. Further experiments have confirmed these results, and it is clear that in his case hyoscine alone influences his attacks to any extent. Despite this example, we agree with Marinesco and Radovici [5] that it is especially those patients who have had no experience of hyoscine and kindred drugs who respond best to therapeutic suggestion. As soon as they have learnt at first hand the effects of such drugs, they are influenced by no others. Several of our patients whose attacks could at first be controlled to some degree by suggestion of various kinds, are no longer in the least susceptible to these methods. Besides the actual cutting short of attacks, psychical factors have a considerable influence in their complete prevention. Thus, one patient whose crises occur several times a week in the afternoon, has never been known to have one on

dance days, whilst another exhibits the same freedom from attacks on days when there is physical drill. Isolated incidents such as these would be quite wrongly interpreted if they were taken to point to malingering. The intensity of the attack appears to have little relation to the effect of psychical factors, and we have at times been able to cut short the severest crises by therapeutic suggestion, whereas at others quite mild attacks in the same patient were completely uninfluenced by such means.

PATHOGENESIS.

Physiological anatomy of conjugate movement.—It is not proposed to attempt a full description of the physiological anatomy of conjugate deviation. The literature on this subject is extensive, and as no two authorities agree as regards details, only a short summary of the more important views will be given.

Higher centres for conjugate deviation.—Conjugate deviation not only responds to volition, but can also be a reflex response to vestibular, visual, auditory, tactile and proprioceptive stimuli. Starting from above downwards, there is a definite area in the second frontal gyrus which appears to be concerned only with voluntary movements, whilst other cortical centres for conjugate deviation have been described by Ferrier in the angular gyrus, and by Schäfer in the visual area of the occipital lobe. Knoll and Topolanski found that electrical stimulation applied behind the posterior commissure produced conjugate deviation of the head and eyes to the stimulated side, and later Graham Brown showed that stimulation of the mid-brain in front of the posterior commissure brought about a deviation to the opposite side. Muskens [6] considers that the fibres subserving this lateral conjugate deviation are pallidofugal, passing by Forel's bundle to posterior commissural supravestibular nuclei, and he considers it the main tract for lateral locomotion and lateral deviation of the eyes. He and others [14] hold that the fastigial nucleus (nucleus tecti of cerebellum) is a primary vestibular centre concerned in the movements of falling backward and looking upward, and that the centre for falling forward movements is near the raphe of the medulla oblongata [7]. He considers that the frequent combination of tonic lateral positions of the eyes with the upward and downward position points to the lesion being where the fibres involved in these two forms of forced movement come close together, viz., just in front of the posterior commissure near the median line, i.e., in the metathalamic region.

Oculomotor nuclei.—The oculomotor nuclei lie in the grey matter of the floor of the aqueduct of Sylvius. Le Gros Clark [3], from a study of their comparative morphology, is of the opinion that the functional elements of the oculomotor nuclei are more probably arranged dorso-ventrally than antero-posteriorly or from above downwards, and suggests that much of the confusion amongst different workers is due to a non-recognition of this fact. He further infers that there is a localization of movement rather than of individual muscles in these nuclei, inward movement or convergence by the internal recti being represented in the paramedian group of cells (nucleus of Perlia) [9], dorsal or upward movement in the dorsal group, and ventral or downward movement in the ventral group. This certainly harmonizes the otherwise divergent views of many observers and agrees with his findings in the field of comparative anatomy. It should be noted, however, that some observers [8] actually reverse these localizations.

Associational and reflex apparatus.—More important in the present context than this probable anatomical localization of cells subserving conjugate movements must be the association fibres which distribute the impulses necessary for these movements. Amongst the most important of these is the dorsal longitudinal bundle which connects the motor nuclei of the ocular nerves with Deiters' nucleus (vestibular); the ascending ventral columns of the spinal cord (proprioceptive); fibres from cells in the tegmentum and the anterior corpora quadrigemina (visual reflexes) which can be traced anteriorly into the subthalamie region and, according to Fraser, into the thalamus itself. Conjugate lateral movements of the eyes are regarded by most authorities as being subserved by a mechanism distinct from that of vertical movement, and this might be expected from the very different combination of muscles used in the two phenomena. The most generally accepted view is that fibres arise in the abducens nucleus and ascend in the dorsal longitudinal bundle of the same or of the opposite side to reach the oculomotor nucleus, and pass out with the third nerve to the opposite internal rectus, thus explaining the invariable working together of the external rectus of one eye and the internal rectus of the other eye [2]. Another hypothesis, which fits the known facts better and is supported by Gordon Holmes, postulates a supranuclear centre in the region of the abducent nucleus which receives impulses from all sources which can cause conjugate deviation of the eyes to the same side. To this centre come voluntary impulses from the opposite frontal centre, visual and auditory reflexes from the corpora quadrigemina, vestibular reflexes

through Deiters' nucleus, and proprioceptive stimuli from the muscles of the head and neck. In this supranuclear centre these impulses are correlated and co-ordinated, and pass on by efferent fibres for the stimulation of the motor nuclei of the corresponding internal and external recti muscles and for the reciprocal inhibition of their antagonists. Clinical evidence in favour of this hypothesis is seen in cases on record, where these various fibres of different function have been injured separately with, in some patients, abolition of the reflex of turning the eyes following labyrinthine impressions, while power of voluntary deviation remained intact, and in others a reversal of this phenomenon. In the same way can be postulated a supranuclear mechanism for upward and downward movements of the eyes. One hypothesis is that this is situated in the anterior corpora quadrigemina, another that it is in the tegmentum or in the central gréy matter around the aqueduct of Sylvius.

General considerations:—In the isolated cases reported in the literature no attempt has been made, as a rule, to discuss the pathogenesis of these attacks. In the somewhat analogous respiratory anomalies the suggestion was frequently made that these were merely hysterical manifestations. No one, so far, seems to have put forward this untenable hypothesis in connection with the oculogyric crises, but as several continental writers [13] [16] favour the view that they are what they call "hysteriform" in character, it would be as well to say a few words on this theory. They do not deny an organic substratum, but consider that the resultant phenomena are produced by the same mental and physical mechanisms as are the grosser physical manifestations of hysteria, such as anæsthesia, paralyses, tics, &c. They maintain that the original onset of the crises in each patient is probably always due to a superadded factor of psychic importance, e.g., a strong emotion, physical or intellectual fatigue, or, and this they consider very important, mental contagion from witnessing a crisis in a fellow patient. In our series of cases this has been the exception, the majority of the patients finding it very difficult or impossible to say when they first experienced a crisis. These authors stress the effect of suggestion in precipitating attacks, and of therapeutic persuasion in cutting them short. Here, again, our experiences do not agree, as we find suggestion quite powerless to initiate an attack in the majority of our patients, and therapeutic persuasion a very variable weapon in cutting them short. There is manifestly a considerable psychical disturbance associated with many of the attacks, just as epileptic fits, attacks of migraine, sea-

sickness, &c., are accompanied and often preceded by similar emotions. It appears to us more reasonable to class these disturbances as part of the attack than as the responsible agents, although it is admitted that emotion, fatigue and excitement may have at times a precipitating effect. This is only to be expected if the hypothesis about to be put forward be a correct one. Unlike our patients, the cases met with by these authors would appear to have contraction of the neck muscles in practically every case, and very frequently the trunk and limbs are also involved, bizarre attitudes being common during the crises. In one case described the oculogyric crises alternated with attacks of hysterical spastic paraplegia lasting for a quarter to half an hour, attacks which the authors say could often be terminated by simple suggestion or injections of distilled water [16]. One would imagine that it must be extremely difficult in such a case to say that the cessation of so short an attack was due to the treatment. It must be granted that there is undoubtedly a similarity between the results of precipitating and inhibitory factors in encephalitis and pithiatism. This has already been pointed out by Turner and Critchley [12] in their study of encephalitic respiratory disorders, and with them we would emphasize that this similarity should not be strained. If these phenomena in our patients are to be regarded as somewhat similar to hysterical manifestations, it should be in the sense that oculogyric crises and analogous encephalitic phenomena point very strongly to hysteria having a physical basis and not being the purely psychological disease it is usually considered. It is not necessary to postulate gross histological changes in and around the basal ganglia in hysteria, but subtle biophysical or biochemical changes in this region may well be present. Variability of symptoms depending on suggestion and emotional factors is by no means confined to hysteria, but is present in practically all organic diseases of the nervous system in greater or less degree. It does not, therefore, seem necessary to postulate or emphasize a psychological origin for these phenomena when they appear in encephalitics any more than when they are found in other organic nervous disorders.

Can we find any organic explanation for the increased suggestibility of the encephalitic? Whilst our cortical centres and their centrifugal paths are intact, we react to external stimuli after an intellectual elaboration by an adequate voluntary movement or by a motor inhibition, in either case arriving at a definitely pursued end. When a functional or organic alteration upsets the normal harmony, the reaction of the individual to the same stimuli reveals a pathological condition. There

is no doubt that the diffuse lesions of the extra-pyramidal system and of the higher vegetative centres set up a new state of function. Lesions of the basal ganglia and neighbouring grey matter must be held responsible for the Parkinsonian rigidity, the slowing and abolition of automatic movements, and the abolition of mimicry and of emotional expression. And in the same way there is little doubt that the lesions of these same centres and of their connections with the cerebral cortex also cause interference with cortical control with resultant psychical disturbances in these patients. Here Pavlov's researches on the conditional reflex have some bearing. He found that lesions of the cortex cause a much greater interference with the inhibitory than with the excitatory impulses, an important fact when it is remembered that many encephalitics have diffuse cortical lesions in addition to the more usual lesions elsewhere. The inhibitory cortical fibres in the encephalitic being thus partially destroyed, external stimuli reaching the subcortical centres are more easily translated into the movements subserved by this part of the brain. The lesions of these basal centres can, therefore, be regarded as the anatomical basis of the psychic phenomena and especially of the increased suggestibility of these patients. The various tonic crises which appear spontaneously in our patients, whether they be striatal fits, ocular spasms or respiratory crises, seem to us to be an expression of this same abnormal functioning of certain subcortical centres, and the varying types of crises found are due to different parts of the area being affected. Two of our encephalitic patients have had fits of extra-pyramidal type, and in spite of Collier's [1] arguments against this type of epilepsy, we agree with Spiller [10], Sterling, and those others who are of opinion that it is due to lesions in the subcortical centres. This same mechanism of liberated function explains equally well the myoclonias due to liberation of the bulbo-medullary motor centres, and the respiratory anomalies due to liberation of the respiratory centres. The occasional appearance of these crises following mental contagion finds a ready explanation in this same cortico-nuclear disintegration with the interruption of the cortical inhibitory fibres. In the same way abnormal suggestibility due to the interruption of the cortico-thalamic inhibitory fibres tends to emotional facility, sometimes seen in an exaggerated form as spasmodic laughing and crying. We can also conceive that a similar partial independence of the motor centres related to standing, walking and other such phenomena, is at the base of the strange paradoxical reactions found in some encephalitics. It is probable that this same mechanism of cortico-

nuclear disintegration governs all phenomena of suggestion, and that in hysteria the afore-mentioned biophysical and biochemical disturbances favour the appearance of this exaggerated subcortical functioning. Suggestibility is the expression of a dynamic state impossible to define with particularity in the present state of our knowledge, but one feels that the study of the encephalitic is likely to prove one of the most fruitful fields in the elucidation of this problem.

Distinct from the lesions causal of this increased suggestibility, we must also postulate lesions which determine the type of subcortical fit taking the form of oculogyric crises. If there are separate supranuclear mechanisms for lateral and for vertical conjugate movements, then the lesion causal of oculogyric crises probably does not lie in any of the supranuclear centres, but in some higher associated mechanism. We are led to presume this from the fact that not only may the eyes take up any position in different attacks, but that even in one and the same attack they may change from the lateral to the vertical position or vice versa, or in some cases to staring straight ahead. In one of our cases (Case 2) the position of the eyes on rare occasions was one of convergence. Such varying positions would scarcely be found if the lesion were limited to one or other supranuclear centre subserving certain movements only of the eye; and it is unlikely that in these cases there are various lesions in the different supranuclear centres. The inhibitory influences normally coming from the cortex being, as we have seen, interfered with, the other impulses which act on the conjugate mechanism find it easily influenced. Here we would state that we cannot agree with Muskens in neglecting the proprioceptive, auditory, visual and vegetative reflexes which act on the supranuclear centres and in regarding the vestibular apparatus as the only one involved. This he does by identifying the crises with the forced movements and forced positions seen in the lower quadrupeds after lesions of the supra-vestibular structures. He lays emphasis on the fact that the French school of neurologists have reported cases, illustrating all varieties of forced movements and forced positions, which from animal experiments have been postulated as being likely to occur with partial lesions of the supra-vestibular centres near the posterior commissure and of their palæostriatal connections. As already stated, our clinical findings do not agree concerning the prevalence of these associated movements. Even if they are only secondary or associated phenomena, their occurrence does not show that the original disturbance causing the ocular spasms is in the vestibular system. Also it is always dangerous

to draw conclusions from experimental work in animals which is still far from being proved. His contention that the lesion is in the metathalamus cannot therefore be accepted as final, and more work is necessary before the causal lesion can be assigned to any definite area or areas. Here it may be mentioned that Levy, Hunt, Vogt, Stern and von Economo think that forced positions in the vertical plane point to lesions in the corpus striatum, and that Tritiakoff, Marinesco, Goldstein, Claude, Holman, MacKinlay and Gowan, on various grounds, place the lesion causal of the crises in the body of Luys.

In suggesting the above hypothesis we do not wish to appear dogmatic. Theorizing is always tempting, but as we do not propose to bring forward evidence in support of any other views, we will merely mention two which appear to us to possess attractive possibilities. Thus, we consider it quite feasible that the metabolic dyscrasia known to be present in chronic encephalitis leads to the setting free of substances which act on the nervous system in the same manner as convulsant poisons. Or, again, we may be dealing with a local vasomotor spasm; and in support of this there is the well-recognized disturbance of the autonomic system in the encephalitic, as seen in the vagotonia of Parkinsonism.

PROGNOSIS.

No definite prognosis as to how long the crises are likely to persist can be given in any individual case, but in a considerable proportion the crises tend to disappear, or become very much less frequent and severe, after treatment by hyoscine. In our series of twenty-three cases, sixteen have attained complete freedom from, or very marked diminution in the frequency and severity of, their crises. This improvement is maintained in six of these patients, even when hyoscine is withdrawn; in five the crises return on omitting hyoscine, and in the remaining five withdrawal of hyoscine has not yet been tried. In five who have been on hyoscine for a considerable time the crises, which are in each case infrequent and mild, have appeared since the administration of this drug was begun. These crises are apparently uninfluenced by hyoscine or any other form of medicinal treatment, but it is of course possible that their attacks might have been more severe were it not for the influence of the drug. One case who had mild staring attacks before the administration of hyoscine still remains unaffected, while the remaining case has been admitted too recently to be classified here. Thus it will be seen that only one out of eighteen patients whose

attacks developed before hyoscine treatment was given remains uninfluenced, compared with sixteen who show undoubted benefit. It is noteworthy that the six cases which at one time were very severe have all progressed very favourably, and that two of them are very much improved, even when hyoscine is withdrawn. The mild infrequent types are relatively the more intractable. The improvement or otherwise as regards these crises shows no correlation to the other symptoms of the disease, and seems to be quite independent of the general progress of the encephalitic process. It may be that the improvement has been effected by a natural process—perhaps an irritative lesion in the brain has become inactive, and that even without hyoscine the spasms would have disappeared. In this respect it is interesting to note that Turner and Critchley [12] found that nearly 50 per cent. of encephalitic respiratory anomalies showed spontaneous cure after a few years. On the other hand, it is possible that the hyoscine, by preventing the attacks over a considerable period, ultimately breaks the reflex "habit," so that later it can be withdrawn with impunity, an action similar to that which appears to be operative in some cases of epilepsy treated with bromides or other sedative drugs.

The second question in prognosis which arises is as to what significance, if any, the onset of oculogyric crises has on the disease as a whole. Should such crises be regarded as making the general outlook for the patient more serious, or should they be regarded more as an intercurrent complication having little or no general prognostic significance? From our experience we incline to the former view. We have found nothing to suggest that these attacks portend a more rapid progress of the chronic encephalitic process, though their onset does afford a reminder that we are dealing with an actively progressive condition. But we would suggest that the real significance of these crises is to be found in the relatively high proportion of these patients who ultimately require certification. Though histological proof is so far lacking, we are probably safe in assuming that when the encephalitic process spreads to the higher centres of the brain, psychotic symptoms become a definite possibility. The proportion of certified encephalitics who have oculogyric crises is certainly higher than amongst non-certified cases, and this we think may be due to the fact that the crises and many of the psychoses result from lesions causing loss of cortical inhibition. The onset of these attacks points to an active spread of the encephalitis, and the possibility of psychotic symptoms must then be borne in mind in giving any prognosis.

THERAPEUTICS.

As in Parkinsonism, the atropine group is unrivalled in its effect, and the majority of cases can be kept free from crises over long periods by judicious use of these drugs. The greatest measure of success is obtained by subcutaneous injections of hyoscine. After very extended trial under careful observation, we have come to the following definite conclusions regarding the use of drugs in Parkinsonism. Belladonna and stramonium can be discarded, as in the few cases where they give any appreciable benefit better results can be obtained from hyoscine by the mouth, or genoscopolamine. Of these two the latter is more generally useful and should always be tried before resorting to injections of hyoscine. With very few exceptions, cases which benefit by these oral methods benefit still more from hyoscine given hypodermically, but for obvious reasons this should only be resorted to if the improved results are great enough to warrant it. In the advanced cases it will be generally found that the injections are infinitely superior and therefore justified. It is important that the smallest efficient dose should be discovered by experiment in each case, and we have even found $\frac{1}{100}$ gr. hyoscine hydrobromide by the mouth every other day sufficient in some cases. The majority of our advanced Parkinsonians require $\frac{1}{100}$ gr.— $\frac{1}{75}$ gr. hypodermically twice or thrice daily. The greater efficacy of injections in oculogyric crises is even more noticeable, and here genoscopolamine has proved rather less successful than hyoscine by the mouth. Therapeutic suggestion is generally to be avoided. Though sometimes successful at first, it is unlikely that the patient will respond to this form of treatment for long, as encephalitics are notoriously alert concerning their treatment and are very quick in finding out if they are being tricked. They are then hurt at the way they have been treated, and are inclined to lose faith in the physician and any treatment he orders. For this reason our experiments with therapeutic suggestion have been as few as possible.

SUMMARY.

(1) Oculogyric crises are unknown apart from epidemic encephalitis, and it is only of comparatively recent years that they have occurred. In our series the earliest case commenced in 1923, and the earliest epidemic which led to a case was that of 1919. The shortest interval between the acute attack and the appearance of the crises has been a few months, and the longest eight years.

(2) These crises are not associated with any particular mental type of encephalitis, but so far they have not been described in a non-Parkinsonian case. Other ocular symptoms are not more frequent than in the ordinary encephalitic without crises.

(3) The crises are in the nature of tonic seizures and need not be confined to the eye muscles, a more or less co-ordinated spread to the muscles of the head and neck being not uncommon. Physical pain is an unusual concomitant, but psychological distress of various kinds is very common.

(4) The eyes may become fixed in any position, and this position may change during a crisis, or from one crisis to another. In one case the eyes took up a position of forced convergence, and in three a fixed stare to the front has been observed. This variability is important in determining the site of the lesion.

(5) The duration of the attack varies from a few seconds up to several hours, and attacks in the same patient may vary considerably in this respect.

(6) The majority of patients show a predilection for certain times of the day, and this is doubtless to be correlated with the effect of fatigue and emotion as determinants of attacks. In the majority of attacks no precipitating cause can be found.

(7) It is occasionally possible to shorten or prevent attacks, and suggestion is the most potent agent in this respect. Each patient usually finds some means of allaying the discomfort incident to the crisis, lying down with eyes covered being the most common.

(8) It is misleading to regard these crises as hysteriform in nature. The undoubted similarity between the results of precipitating and inhibitory factors in hysteria and encephalitis should not be strained, as variability of symptoms depending on suggestion and emotional factors is not confined to hysteria, but is present to some extent in practically all diseases of the nervous system.

(9) The increased suggestibility of the encephalitic is due to an interference with normal cortical control and a cutting off of its inhibitory influence.

(10) The abolition of cortical inhibition explains the release phenomena of different subcortical centres manifested clinically as tonic fits, ocular spasms, respiratory crises, myoclonias, emotional facility, paradoxical reactions, &c., the particular manifestation depending on the site of the lesion.

(11) The causal lesion of oculogyric crises lies in associational

mechanisms situated above the four supranuclear centres subserving conjugate movements, the theory being accepted that there is a supranuclear centre for lateral conjugate movements, and one for vertical movements on each side.

(12) The effect of emotion on the crises is probably indirect, brought about by an inhibition of the already enfeebled inhibitory fibres from the cortex.

(13) In a certain proportion of the cases the crises tend to disappear with time, and this is especially so in cases treated with hyoscine.

(14) A large proportion of encephalitics who suffer from oculogyric crises subsequently require certification, a fact which should be correlated with the loss of cortical inhibition in these crises and in encephalitic psychoses.

(15) Hyoscine administered hypodermically is the most generally useful method of treatment in this, as in other Parkinsonian phenomena, but it should only be used under careful supervision and in selected cases.

REPRESENTATIVE CASES.

Case 1.—J. W. B., male, aged 15, was admitted to West Park Mental Hospital, August 16, 1927. His encephalitis appears to date from 1923, and in 1926 deficient cortical inhibition became prominent in a liability to fits of uncontrollable temper, impulsive violence and frequent threats of suicide. This led to his certification in 1927, when he was admitted to Warwick County Mental Hospital. During his three months' stay there he is reputed to have been dull, listless, vacant and of very slow cerebration. Parkinsonism appears to have advanced quickly in 1926, and on admission here was so marked as to render him quite helpless and unable to stand unaided. There was a left-sided hemiplegia, including the left side of face. Cogwheel rigidity was well marked. The head was held flexed on the chest and turned to the left. No tremor was observed. Voice was slow, monotonous and very indistinct; salivation was excessive.

Ocular system.—The pupils are equal, regular and react normally to light and on accommodation. No deficiency of convergence is present. Eye movements are fairly smooth, but there is some difficulty in looking to the extreme right. Upward movement is good, but there is a total inability to wrinkle the brow. Some blepharospasm is present on closing eyes. There is no strabismus, nystagmus or ptosis. Diplopia is complained of during oculogyric crises. The fields of vision and fundi are normal. On admission his apathetic tendencies were not in evidence, and his most prominent mental symptoms were bradyphrenia tinged with a mild degree of reactive depression. An immediate mental and physical improvement was effected by injections of hyoscine, 1 to 2 gr. once a day, and he was very shortly able to get about, feed and dress himself, and generally take an interest in life. He is now very active and can

walk and run well, although with a limp. Rigidity of neck muscles and carriage of head was rather intractable at first, but has now been much improved by massage and electricity. On the withdrawal of hyoscine, even if for a single day, he reverts to a condition of helplessness and misery similar to his state on admission.

Oculogyric crises.—These first started about a fortnight before he left Warwick County Mental Hospital, in May, 1927. The patient noticed that he was occasionally unable to follow the lines of a book he was reading, but if he got up and walked about for a while his eyes would recover. On admission to West Park crises were very severe, frequent and of many hours' duration. A complete inhibition was rapidly effected by means of injections of hyoscine. On withdrawing the drug for a week, regular and severe attacks recommenced and lasted from a few minutes after waking until about 6 p.m. The deviation was sometimes upwards and to the left, and at others downwards and to the left. The head was turned towards the left and held rigidly in a position of flexion or extension, depending upon the position of the eyes. The omission of hyoscine even for one day invariably results in the appearance of ocular crises. There is no local pain or discomfort, but considerable mental distress is evident. Diplopia is sometimes complained of during attacks, and shutting the eyes is impossible. Lying down, covering the eyes or blinking have no effect upon the spasms. Soon after admission an attack was cut short by the inhalation of amyl nitrite, but this has never succeeded since that occasion. Several other forms of therapeutic suggestion, including injections of water, have been tried and the results have been invariably unsuccessful. Vestibular tests were carried out actually during a crisis. Both in the rotatory and the caloric tests giddiness and vomiting were very easily produced. It was found that no nystagmus could be evoked away from the side to which the eyes deviated (i.e., the left), that is to say, after rotating the patient to the right nystagmus to the left was observed, but after rotation to the left there was no nystagmus. The caloric tests similarly failed to produce nystagmus to the right. Between the crises the vestibular reactions were normal.

Case 2.—E. B., a girl, aged 14, was admitted to West Park Mental Hospital, on December 3, 1927. She had her acute attack in April, 1924, and Parkinsonism appeared in the following year. Her condition progressed and she became increasingly psychotic and difficult to manage, with symptoms pointing to "release" from cortical inhibition. Suicidal tendencies developed and she was admitted to West Park. She showed a fairly advanced state of Parkinsonism ($R > L$), with coarse tremor, monotonous speech and excessive salivation. She was on the whole bright and cheerful, except around the period of her oculogyric crises.

Ocular system.—The right pupil is larger than the left. Reaction to light is good and accommodation reflex and power of convergence only slightly defective. Eye movements are jerky and ability to look upwards is impaired. She is quite unable to wrinkle her brow. A few nystagmoid jerkings are noticed on looking to the extreme sides. Some blepharospasm is occasionally seen but

there is no ptosis, strabismus or diplopia. Fields of vision and eye grounds are normal.

Oculogyric crises.—These were noticed early in 1927, at Winchmore Hill, but the patient states that she had her first attack about three months after her illness began. She describes how she was playing with a girl friend at putting their faces in peculiar positions, and that on copying her friend's effort she got her eyes up and could not get them down again until supper time (about four hours). On admission to West Park the attacks were severe, and at one time she remained with her eyes fixed in a tonic spasm throughout several days, with only brief and infrequent intermissions. Her sleep, however, was not interfered with, and during this the condition relaxed. For a few days not even injections of hyoscine had any influence on the attacks, but at length they stopped of their own accord. A few days later they recommenced, and since then they have been fairly well controlled by hyoscine. The attacks were associated with extreme distress and often screaming. She liked to go to bed and put her head under the clothes to assist her to close her eyes, a performance of great difficulty to her. If bed were not allowed immediately she would scream and bang her head on the floor or on the furniture in order to get her way. The deviation was straight up, or up and to either side. Of late her crises have been few and mild, but about half an hour before the injections of hyoscine she starts blinking rapidly and persistently, at the same time walking round the ward with her head hyperextended and an extremely worried expression on her face, and constantly asking the nurses whether she is looking cross-eyed. On two occasions she has been observed with her eyes fixed in a position of extreme convergence. This type of crises, which has not been seen in any other case, brings with it an exceptional distress. The patient cries bitterly and is genuinely frightened and miserable. Vestibular tests were carried out during a crises with results similar to those in Case 1.

Case 3.—H. R. D., male, aged 22, was admitted to West Park Mental Hospital, on April 12, 1928. His primary illness, four years ago, was of gradual onset, and he was able to work up till two years ago. On admission he showed a moderate degree of Parkinsonism, with characteristic speech, facies, posture, shuffling gait and sialorrhœa. Mentally he belonged to the behaviouristic group, with the typical encephalitic temperament. His conduct changes were closely associated with his oculogyric crises, and pointed very strongly to a common factor being present in both phenomena, the factor in our opinion being impairment of his power of cortical inhibition.

Ocular symptoms.—His pupils are equal, but irregular in outline; they react normally to light, but very poorly on accommodation; there is practically no power of convergence. Movements are slow and jerky with some impairment of the power of looking up. Slight blepharospasm is present, but no nystagmus, strabismus or diplopia. Double ptosis of varying degree may be seen. Wrinkling the brow is extremely defective. The visual fields and eye-grounds are normal.

Oculogyric crises.—These started two years ago and have recently occurred

three or four times a week. They are accompanied by fits of violent and uncontrollable temper, in which he uses foul language and resorts to screaming, biting and kicking. The onset of excitement usually anticipates the crisis and always outlasts it considerably. The average attack starts in the afternoon and lasts till nightfall, but during this period the eyes may only be fixed for about an hour. The deviation is usually straight up, but may be up and to either side during the same attack. During the crises there is difficulty in shutting the eyes, but no actual pain is experienced. During the first eleven days after admission he had six attacks of excitement with ocular spasms. He was then put on genoscopolamine pills, and during a period of three and a half weeks he had only three attacks of excitement, and nothing but momentary fixation of the eyes.

Case 4.—D. D., male, aged 17, was admitted to the Manor Institution on February 20, 1925. In 1919 he had an acute attack of encephalitis, followed some years later by conduct changes, irritability, moral deterioration and occasional epileptiform seizures. He was from all accounts an especially bright boy before his illness, and intelligence and other tests show that he continued his mental development for some time after the onset of his encephalitis. He is now of the apache type with the typical encephalitic temperament and evidence of a certain degree of intellectual deterioration. He is irritable, quarrelsome and lacking in control, and has been found attempting indecent exposure and abnormal acts. His Parkinsonism is confined to the upper part of his body, and is the least marked of all our cases.

Ocular system.—The pupils are irregular and unequal ($R > L$), they react briskly to light but sluggishly on accommodation. Convergence is only fair. The ocular movements are fairly smooth and rapid, but there is an ill-sustained rapid oscillation on looking up and a few nystagmoid jerkings on looking in other directions, especially up and to the right. The range of upward movement is defective, but wrinkling the brow is fairly well performed. No blepharospasm or ptosis is present. The visual fields and fundi are normal.

Oculogyric crises.—These first occurred as early as 1923, about the time his apache tendencies first developed. He describes how he used to have attacks when coming home after a hard day's work on a farm. On admission they used to occur about once a week, but increased in frequency until they became almost daily incidents. The position was invariably up and to the left, and the time of day always late afternoon or evening. They annoyed him and made his eyes ache, but caused no real distress. He was able to stop them temporarily by tightly screwing up his eyes. They have now been reduced to a minimum by means of genoscopolamine and are very rarely seen. At one time threats of removing certain privileges were successful in producing a strong enough voluntary effort to check an attack, but later these means became useless.

Case 5.—A. W. A., male, aged 22, was admitted to West Park Mental Hospital on February 7, 1928. He had a mild primary attack six or seven years previously. Parkinsonism and oculogyric crises were first noticed about

three years ago, while fits of excitement and temper began to occur several months later. He is of the bradyphrenic type and exhibits the characteristic childish, sympathy-craving temperament. Except for acute excitement associated with his crises, there are no definite conduct disturbances; he exhibits a mild degree of Parkinsonism and bradykinesia.

Ocular system.—The left pupil is oval, but the reactions to light and accommodation are unaffected, and convergence is normal. Movements are rather jerky and there is considerable deficiency in the upward range. Wrinkling the brow is much impaired. No nystagmus, ptosis, strabismus or diplopia are present. Blepharospasm is very much in evidence and blinking attacks occur. Fields of vision and eye grounds are normal.

Oculogyric crises.—These are said to have come on about four years ago and were noticed by the patient's father and mother three years ago. They occurred about twice a week, and were often associated with excitement and temper which usually preceded as well as accompanied the attack. The patient states that his first attack occurred while he was on the stairs at home, and he can suggest no cause for it. He covered his eyes with a mackintosh and lay down and the crisis passed off in ten minutes. During the first year or two no excitement was evident. There is no pain and only a slight feeling of discomfort. There is, however, considerable distress, the patient describing a sensation that he is going blind. Since admission he has had several fits of violent excitement and temper lasting one and a half hours, sometimes with and sometimes without fixation of the eyes. Hyoscine injections are successful in cutting short or preventing attacks.

In conclusion, we take this opportunity of thanking Dr. Norcliffe Roberts, Medical Superintendent of West Park Mental Hospital, and Dr. E. S. Littelljohn, Medical Superintendent of the Manor Institution, for allowing us to publish the cases, and Dr. F. Golla for his unfailing interest in our investigations.

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OBSERVATIONS UPON THE VASCULARITY OF THE HUMAN OCCIPITAL LOBE DURING VISUAL ACTIVITY.

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FOR many years it has been suspected, though never adequately proved, that the rate of flow of blood through the brain increases as a result of sustained mental effort. This belief is in harmony with the increase in the metabolic exchange of human beings which appears to occur during vigorous intellectual activity [Becker and Olsen, 1914; Day, 1923; Gillespie, 1924; v. Liebermann, 1926]. Such an increase, however, may be due in part, or possibly wholly, to the increased muscular tension developed during sustained mental effort, and while precautions have been taken to exclude this factor [see especially Gillespie, 1924], observations upon the point are still equivocal [for early observations and a discussion of the literature, see Benedict and Carpenter, 1909].

Recently evidence bearing upon the vascular supply of the brain has been adduced from quite a new angle. It is well known that some portions of the grey matter of the central nervous system are much more richly supplied with capillaries than other parts. In a series of important investigations Craigie [1921, 1924, 1925, 1926, 1927] has found that the vascularity of the brain-stem and cerebellum of animals is much less at birth than after five days of life or than at maturity. Moreover, the relative vascularity of the various centres within the brain-stem does not differ much at birth, while marked differences occur in adults. A similar, though slightly less marked, increase in vascularity occurs in the cerebral cortex of rats during the first days of life. Craigie believes that the vascular richness of the various parts of the brain is related to functional activity, and that the increase which he has found in localized regions is due to increasing metabolic demands of those parts associated with activity, the nutritional requirements for functional activity being greater than for growth. In the medulla the sensory nuclei are more richly vascularized than the motor, a relation which

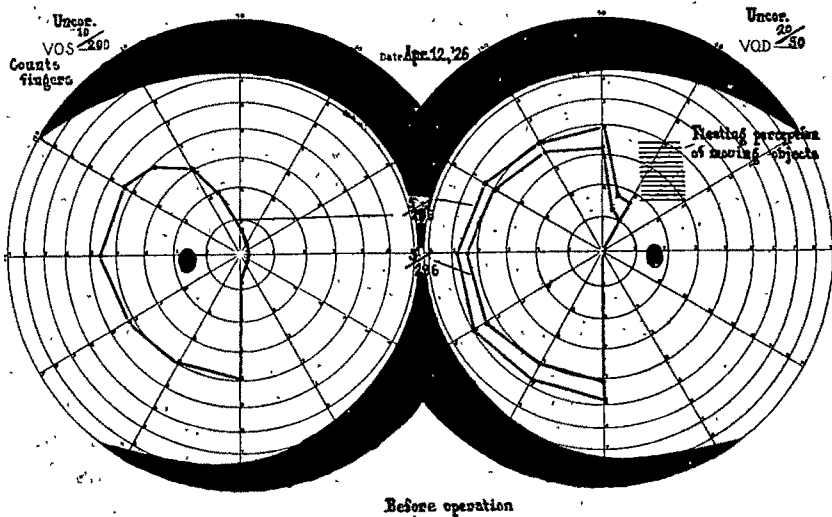
undoubtedly is to be accounted for by the more continuous activity of the sensory neurons as contrasted with the less frequent activity of the motor neurons.

It becomes, therefore, a problem of great interest to know whether, during the reception of sensory impulses, the centres affected become more richly supplied with blood than when resting. Also, if such an increase occur, one would like to know whether it is local or due to a generalized increase affecting the whole brain. These two problems have lately been investigated by Cobb and Talbot [1927], who have studied the magnitude of the capillary bed in the motor cortex in the visual area and in the olfactory bulbs of a series of animals which, immediately before death, were subjected to vigorous *olfactory* stimuli. The animals were injected at the time of death, and the micrometric method of Vogt applied for estimation of the relative areas of the capillary bed. In the unstimulated animals the olfactory bulbs showed 110 micra of open capillaries per 100,000 cubic micra of brain substance. Ether-stimulated animals, on the other hand, showed 149 micra, while ammonia-stimulated animals showed 171 micra. The motor cortex and the visual areas of the occipital lobe, on the other hand, showed no change under olfactory stimulation. These observations, though possibly open to the objection that an irritating stimulus was used, are significant, and suggest that vigorous sensory stimulation of a given centre in the brain is associated with an increased blood-supply to that centre.

The following case, recently under observation at the Peter Bent Brigham Hospital, Boston, Mass., appears to throw further light upon the problem of altered vascular supply of localized areas in the brain during functional activity.

*Case 1.*¹—P. B. B. H. Surg., Nos. 26137 and 29731. Headache, failure of vision with right homonymous hemianopsia; bilateral external carotid ligation; left occipital osteoplastic exploration; disclosure of typical angioma arteriale racemosum, inoperable because of its vascularity; decompression; diminution of subjective symptoms following decompression and X-ray treatment. Clearly audible auscultatory bruit over tumour; increase in intensity of bruit during visual effort.

¹ Further clinical details concerning this case, with full discussion of the pathology of this group of rare and interesting tumours, is given by Cushing and Bailey in their monograph, "Tumors arising from Blood-vessels of the Brain: Angiomatous Malformations and Hemangioblastomas." Springfield: Thomas, 1928 (in press).



Before operation

FIG. 1A.

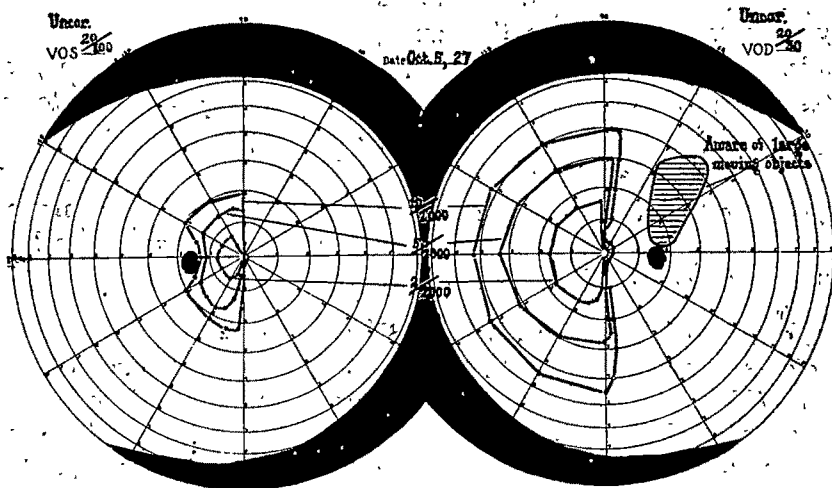
Bruit louder subjectively and objectively
while trying to see off to right side

FIG. 1B.

FIG. 1.—Visual fields, (A) before, and (B) one and a half years after, operation, showing right homonymous hemianopsia with partial sparing of macula. The hemianopsia was incomplete, since in the upper temporal quadrant of his right eye the patient was dimly aware of moving objects. It was when attempting to perceive moving objects to his blind side that the bruit in his left occipital region was most noticeably augmented.

Walter K., a single German-American sailor, aged 26, was admitted April 12, 1926, because of headache and failure of vision. The patient stated that for seven years he had had increasingly severe pain in his left temporal region which, however, had diminished a few months before entry. For five years he had had failing vision, the left eye having been reduced to almost complete blindness, and he had noticed for several months that he could not see to his right side. During the previous six months he had been conscious of a humming noise referred to his left ear. There had been no deafness, dizziness, ataxia or vomiting, and no weakness of any of the extremities.

Physical examination revealed a loud, coarse systolic bruit over the left occipital region, right homonymous hemianopsia with sparing of the macula (fig. 1), left exophthalmus with slight pulsation, bilateral choked disc with evidence of extensive secondary optic atrophy on the left side and early secondary atrophy on the right. There were no other significant neurological findings, except that the pulsation of the left temporal artery was more forceful than of the right. The deep reflexes were equal and active, and there were no cranial nerve palsies. X-ray of the skull (fig. 2) disclosed an area of increased vascularity over the left occipital lobe with slight erosion of the bone in this area. There was also a moderate increase in convolutional markings suggestive of increased intracranial pressure.

At operation, on April 23, 1926, Dr. Cushing, in anticipation of encountering a highly vascular tumour, carried out first a bilateral ligation of the external carotid arteries. On turning down a left occipital bone flap, a large, angry-looking angioma arteriale racemosum of the left occipital lobe was disclosed which extensively involved the visual cortex. The hæmorrhage occasioned by the bone flap was so excessive that the operation had to be abandoned without touching the tumour. A decompression, however, was made. The patient was discharged on May 16 after a normal post-operative recovery, with greatly improved vision, diminution of left exophthalmus and freedom from occipital pain, but the bruit still persisted. After discharge from the hospital he was given two series of deep X-ray treatments, which produced a marked diminution in the intensity of the cerebral bruit. The patient was conscious of this himself, and it was evident to those who examined him. His vision also continued to improve.

Second entry.—The patient re-entered the hospital September 27, 1927, at Dr. Cushing's request, for further observation and possible operation. Examination at this time showed a well-developed man in excellent physical condition, with well-healed bilateral scars on his neck and a pulsating post-operative defect in his left occipital region. The bruit was still audible over the defect, but it had apparently diminished in intensity. There was bilateral secondary atrophy, more marked left than right, right homonymous hemianopsia, complete for resting but incomplete for moving objects, and a concentrically-constricted left temporal field (see fig. 1B). Visual acuity was $\frac{20}{100}$ left, $\frac{20}{30}$ right, uncorrected. His fundi showed tortuous veins and it was observed in his left fundus that, though the veins did not pulsate, there was very little difference in

colour between arteries and veins. On compressing his jugulars the retinal veins could be made to pulsate with ease; the difference in colour between arteries and veins then became somewhat greater. During jugular compression his left temple swelled while his right did not. There were no other significant neurological signs.

Observations on the bruit.—Several days after entry, while testing the patient's fields, he remarked that the noise in the back of his head increased in intensity when he was using his eyes. He said that he

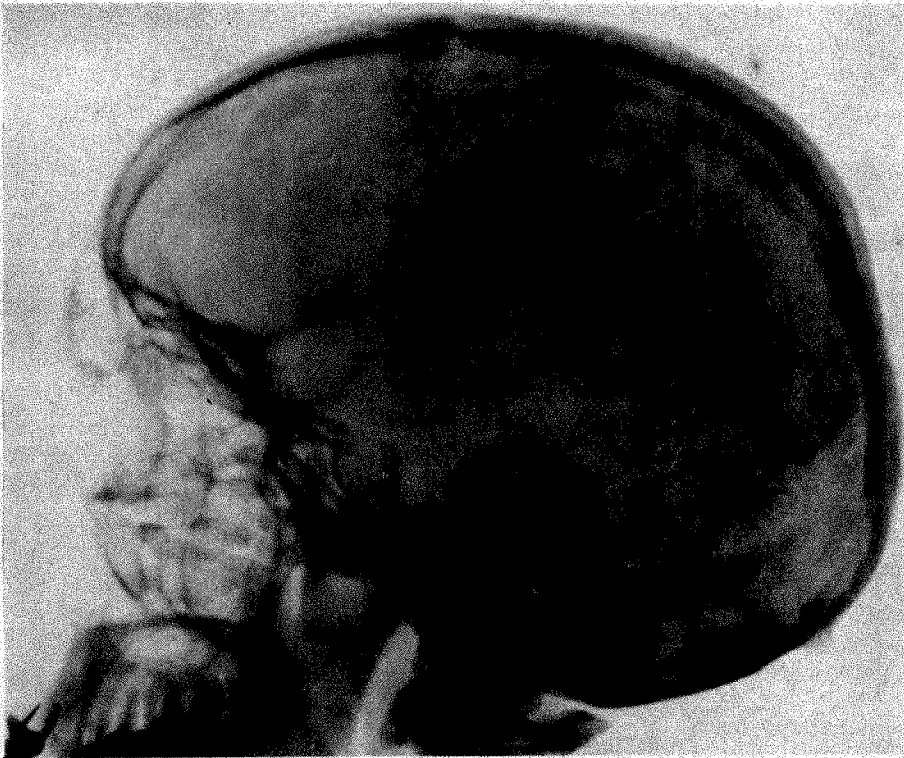


FIG. 2.—X-ray photograph of skull (left) prior to operation, showing area of bony rarefaction in left occipital region overlying the angioma.

had often noticed this during the past several years, but had "never thought much of it." On listening to the bruit, it was obvious that it was much louder than when first examined on the day of entry. Subsequent observations were made during the following week, and it was not difficult to convince ourselves that when the patient suddenly began to use his eyes after a prolonged period of rest in a dark room,

there was a prompt and noticeable increase in the intensity of his bruit. The increase was detectable within twenty to thirty seconds, and if he was permitted to use his eyes for one to one and a half minutes, and then directed to close his eyes, the bruit would continue at heightened intensity for nearly a minute and then gradually subside. The patient was cautioned not to make his muscles tense during the time when his eyes were being tested, and we believe that the only significant additional muscular effort was that of opening and closing his eyes. Simultaneous observations of his blood-pressure during the time that his eyes were being tested gave inconstant results. On one



FIG. 3.—Patient three weeks after operation, showing the region explored. The arrow indicates the point of maximum intensity of the bruit. This overlies the region of greatest vascularity of the angioma.

occasion, during a long session in which his fields were being tested, there was a rise of five to ten points in his systolic pressure (120-125-130). Frequently, however, there was an increase in the intensity of his bruit without any concomitant rise of blood-pressure, and there was no change in pulse-rate. Activity of his other sense organs, moreover, had no effect upon his bruit. Thus, smelling tobacco or vanilla did not influence it, straining to hear the ticking of a distant watch produced no effect, and ordinary quiet conversation was without demonstrable influence. We believe, therefore, that the effect is due to a genuine increase in the vascularity of the region about his left occipital lobe.

As stethoscopic observations on the augmentation of the bruit during visual activity are open to the objections associated with any subjective impression, further evidence was secured by recording the bruit photographically with a microphone and a string galvanometer. The patient was allowed to lie on his stomach in a comfortable position, with his chin resting on the edge of a chaise-longue in such a way that he could close his eyes and open them to read a newspaper lying on the floor. He was permitted to rest in this position in a completely darkened room for five to ten minutes before observation. Records

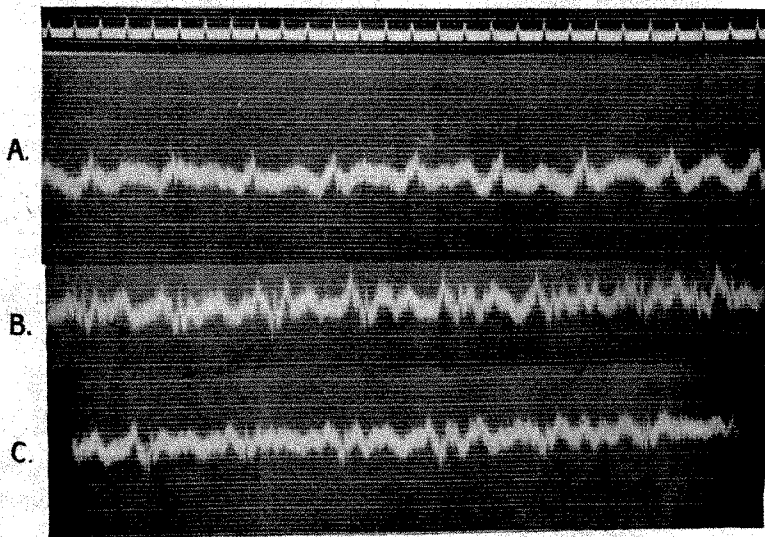


FIG. 4.—Typical electrophonograms of bruit. A, after ten minutes' rest in a darkened room; B, after two minutes' reading of small print illuminated by a single 40-watt tungsten bulb at 5 feet; C, three minutes later, after two and a half minutes' rest in darkened room. Note increased size of main deflections in B and the greater number of secondary deflections. (Telephone transmitter placed directly over point of maximum intensity of bruit on shaved scalp; transmitter in series with Einthoven string galvanometer.) Time above: 0.2 sec.

were then taken of the magnitude of the excursions set up by the bruit, and then the light was turned on the newspaper in front of him and he proceeded to read the smallest type which he was able to see, having been cautioned beforehand not to use his lips or to move in any way. The microphone was placed directly on the back of his head at the point of maximum intensity of the bruit, as determined previously by the use of a bell stethoscope. His head was shaved over the area so as to exclude extraneous noises, such as come from the crinkling of the hair. In one or two records in which he inadvertently spoke, the

voice was transmitted so markedly that the string was thrown into a veritable paroxysm of vibration. When the microphone was placed on other regions of his head the string was absolutely quiet.

Repeated observations with this technique showed that within twenty to thirty seconds after the patient began to use his eyes there was a noticeable increase in the intensity of the bruit. This continued and reached a maximum at the end of one to two minutes (fig. 4). If at this time the lights were put out, the bruit continued very loud and coarse, as judged by the string records, for nearly a minute after the lights were turned off; then it gradually subsided, and at the end of two minutes had returned practically to the resting level (see fig. 4). This observation was repeatedly confirmed.

Critics may object that the magnitude of the sound over an aneurysmal tumour is not an adequate index of circulatory activity. Constriction, for instance, of the arteriovenous communications might lead to an increase in the bruit without an increase of blood-flow. But that this is not the case is evident from the fact that the patient's decompressed area immediately over the angioma, though soft at the beginning of an observation, usually bulged markedly after he had been using his eyes for some time, the position of his body remaining unchanged. It is interesting, also, that jugular compression causes an immediate cessation of bruit. When the jugulars were released the bruit returned with increased intensity for a few seconds and then gradually subsided to normal.

After the patient was discharged (October 14, 1927), he was observed every two to three weeks for five months, during which period he had a series of X-ray treatments directed toward his tumour. At first the treatment seemed to have little effect upon the resting intensity of his bruit, but gradually, after about three to four months, a noticeable diminution occurred. When the patient was last seen (February 28, 1928), the following note concerning his bruit was made on his hospital record:—

"Patient feels since last three X-ray treatments that his bruit has diminished almost to the vanishing point. He now is conscious of it only at night when he lies down with his head on the pillow, but never seems to be aware of it during the day unless he performs some vigorous exercise. Since we showed him that jugular compression caused the bruit to disappear, he frequently checks the sound himself when he thinks it is coming. If present, he can shut it off readily by squeezing his own neck, and is then immediately conscious of its disappearance.

"When patient first entered the hospital this afternoon, the bruit was completely inaudible. Moreover, the decompressed area at his left occipital pole was soft and appeared even slightly sucked in. On previous visits the decompression has always been slightly tense with a moderate bulge. During the forty-five minutes that patient waited, I talked with him the greater part of the time and listened to his bruit, as did also Dr. Bailey, but neither of us was able to detect anything but a most distant and scarcely recognizable sound. His fields were taken at 5 o'clock, and five minutes later the bruit was moderately loud and clearly audible. Patient was conscious of its reappearance as we were taking his fields, especially when trying to see to his right homonymous side. The decompression also became somewhat more full. Dr. Bailey listened to the bruit after the fields were taken, and was quite astonished at the extent of its augmentation. Slight bilateral jugular compression caused the bruit to disappear immediately, and firm compression of his neck (sufficient to abolish his temporal pulse) did not lead to its reappearance. During firm jugular compression the left eye, which is still slightly exophthalmic, pulsated just perceptibly. Jugular compression gave the patient rather a severe headache, so we did not pursue the observation further. The quality of the bruit is altered since it was last heard, it being now low-pitched and machinery-like in quality, whereas before it was high with more over-tones.

"*Visual fields.*—His right homonymous defect is now complete, and appears to have diminished somewhat during the course of X-ray treatments. I fancy that the shrinking up of the blood-vessels in his left visual cortex may have impaired what little functional visual cortex may have remained on that side. It seems extraordinary, however, that the patient still has undoubted vasomotor response on that side during visual effort."

"The *fundi* are essentially unchanged, except for the fact that the veins appear less full than when previously examined. There is marked secondary atrophy of the left and slight secondary pallor of his right disc. The difference in colour between the arteries and veins of the left eye appears to be more marked than before. In other words, this would appear to indicate that there is less arteriovenous communication in his cerebral vessels than previously."

He had further X-ray treatments after this visit, and on June 8, 1928, he wrote: "I have no more noise in my head, even when I use my eyes for some length of time." Evidently the prolonged X-ray therapy eventually produced complete thrombosis of the angiomatous vessels.

INTERPRETATION.

In considering the interpretation of the foregoing observations, we may mention the following additional facts. Careful observations of patient's blood-pressure during visual tests showed that there was no significant increase in his systolic pressure. On one occasion, when a large number of observers were in the room and the patient remarked

that he was getting worked up by having so much done to him, a rise of ten points in his systolic pressure was observed. On this occasion the patient was conscious that his bruit had increased, and he said that when he gets worked up in this way it is apt to stay very loud for ten to fifteen minutes, and this in fact proved to be the case by observation of the intensity of the sounds by auscultation. However, when the patient merely opened his eyes and attempted to read the eye-testing chart, there were no emotional stimuli, and he was cautioned not to move or speak during the period of observation. Under these circumstances there was no elevation whatsoever in his systolic blood-pressure, but there was a noticeable increase in the intensity of the bruit. We gained the impression that it was the effort of trying to discern objects which were just at the limit of his acuity which brought on the increase in intensity of the bruit. Merely shining light into his eyes when he was making no mental effort did not appear to do it. Moreover, the bruit increased very markedly when he attempted to read a paper in poor light, so that we believe that the light *per se* had very little influence upon the results. As to whether the effort of accommodating or moving his eyes was involved in the response, we are unable to say. The effort, in other words, of attempting to discern poorly-lighted or small objects appears to be the most potent stimulus.

It is also significant that auditory and olfactory stimuli did not increase the intensity of the bruit; that is, the response is connected with a process localized in the region of the vascular tumour. This, be it noted, is entirely in harmony with Cobb and Talbot's experimental observations upon the increased vascularity of the olfactory bulbs following olfactory stimuli. They were unable to detect any increase in vascularity in other portions of the brain.

In conclusion, it would seem evident that the observation just described strongly supports the view that localized increase in vascularity of the brain occurs under appropriate sensory stimulation, or, more specifically, it is probable that visual activity in man is associated with an increase in the vascularity of the occipital lobes.

SUMMARY.

A case is described of a man in whom there was a circumscribed angioma arteriale racemosum of the left occipital visual cortex which had produced an incomplete right homonymous hemianopsia. Associated with the tumour was a well-marked auscultatory bruit. When

the patient was at rest with his eyes closed the bruit was distant and weak. When the patient used his eyes for reading, or attempted to perceive objects to his blind side without otherwise exerting himself, a very marked increase occurred in the bruit, detectable both by auscultation and by electrophonograms. Other types of mental effort, such as straining to hear the tick of a distant watch or various forms of olfactory stimulation, had no influence upon the bruit. It would appear that visual effort was associated in this case with increased vascularization of the occipital cortex.

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CHRONIC PROGRESSIVE EXTERNAL OPHTHALMOPLÉGIA.¹

REPORT OF A CASE WITH NECROPSY.

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DIFFERENT forms of external ophthalmoplegia are well known, but in this communication we shall describe an unusual clinical case, the only one, we believe, with necropsy, belonging to a group described in the literature as "chronic, progressive, external ophthalmoplegia."

Wilbrand and Saenger [15] collected thirty-two cases of this form of ophthalmoplegia and, because of the following clinical characteristics, they regarded it as a distinct clinical entity :—

"Bilateral, slowly-progressive paralysis of the external muscles of the eyes develops without any other signs of disease. Years may elapse between the development of the first symptom and the development of complete ophthalmoplegia. The onset is gradual, usually beginning in childhood, seldom in adult life. The rate of progression is variable, but it generally ends in complete external ophthalmoplegia. Ptosis may be the first sign of the disease and may, for a considerable period of time, be the only one. After the ocular muscles become affected, diplopia may be complained of, but this symptom is infrequently noted because of the extremely slow progress of the paralysis, and because it is generally symmetrical. The health of the patient is not affected. It is a striking feature of the affection that no other signs or symptoms develop indicating implication of other organs or other structures of the nervous system."

McMullen and Hines [10] reported three personal observations. (One of the cases, however, showed signs of disease of the central

¹ Read before the meeting of the American Neurological Association, Washington, D.C. May 5, 1928.

nervous system, confirmed at a later examination, so that it can be excluded from the group.)

Discussing the literature, they refer to cases reported since Wilbrand and Saenger's article by Beaumont (twelve cases) and Atland. The characteristics of Beaumont's cases were: (1) Familial; (2) never congenital; (3) slowly progressive; (4) never fatal.

In Atland's [1] case the trouble developed, at the age of 22, in the right upper lid, and at 40 the left upper lid became affected. When seen at the age of 51 the ptosis of the right eyelid was complete, that of the left incomplete, and both globes were immovable.

In discussing the various forms of hereditary ocular paralysis, Collins [5] quoted Gowers' own statement regarding his well-known theory of "abiotrophies," and pointed out that in chronic progressive ophthalmoplegia all the orbital striated muscles became paralysed, but the unstriated intra-ocular muscles invariably remained unaffected, and he emphasized the fact that many of the cases belonging to this group had been watched for long periods of time, and that not one of them had ever developed additional symptoms attributable to the nervous system. For this reason he alluded to the apparent resemblance of the paralysis of these cases to an isolated form of bilateral ptosis described by Fuchs [7] in 1890, and which he thought were cases of primary myopathy. Collins suggested, because of this apparently strong circumstantial evidence, that chronic progressive bilateral ophthalmoplegia might be, in reality, another limited form of primary myopathy and not, therefore, dependent upon alteration of the nervous system.

Wilbrand and Saenger [15] regarded this condition as a disease of the ocular nuclei, while Brouwer [3] thought it was dependent upon alterations of the nerve trunks innervating the extra-ocular muscles. Wilbrand and Saenger, as well as Collins, reviewed the literature of the subject and stated that there had never been a post-mortem examination reported. Since their descriptions were published in the years 1920 and 1922 respectively, a number of clinical cases have been recorded, but we have been unable to find the record of a single necropsy.

The case which we have to record here was carefully studied during the lifetime of the patient by both of us. Only the brain was obtained for examination. The third, fourth and sixth cranial nerves and the optic nerves were cut in cross and in longitudinal sections. The brain-stem was cut in serial sections, and every tenth section was stained with hæmalum and acid fuchsin, and with the Weigert and Nissl methods;

additional sections were stained with toluidin blue and the van Gieson method. Unfortunately, the ocular muscles were not obtained for examination.

Mrs. W. H. C. was first examined in January, 1924, at the age of 81, and was under observation until her death at the age of 84. It was stated by the patient, and also by her daughters, that the right eyelid had begun to droop at the age of 43 (a photograph of the patient was shown to us, taken at the age of 30, in which ptosis was not revealed, but another photograph, taken at the age of 48, showed right-sided ptosis), and soon after this the left lid was similarly affected. It is not known positively what time had elapsed after the onset of ptosis, or even whether the ptosis had preceded the completion of external

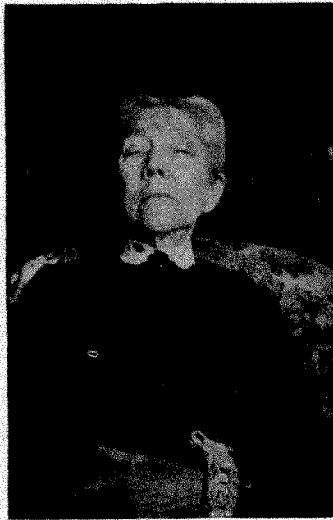


FIG. 1.—Patient, aged 81, showing bilateral ptosis. (Page 3 of paper.)

ophthalmoplegia, for it was not discovered by one of us (Dr. Langdon) until fully developed, when the patient had reached the age of 75. The general health of the patient at that time and subsequently had been very good. She had had no evidence of illness of any kind. Her parents had been normal, and her near living relations and three daughters were in perfect health and, on inquiry, it was stated that no other members of the family had had a similar disease.

Examination revealed complete ptosis of each eyelid; the visual axes were slightly divergent, the pupils measured 3 mm. on each side and reacted promptly to light. The power of accommodation was very feeble, but not entirely lost. The two eyeballs appeared immobile, but on voluntary effort an extremely slight movement of each eyeball, when rotation was attempted in any direction, could be detected. When both eyelids were held open by the examiner

diplopia developed, but when only one eye was held open at a time by adhesive plaster attached to the brow, the patient got on quite comfortably. There were some changes in the lens in each eye; the rest of the media were clear. The retinal arteries were irregular, with some indentation of the underlying veins. The discs were well coloured with clear margins. The fundi otherwise were in good condition. The corrected vision of the right eye was $\frac{5}{20}$ and of the left eye $\frac{5}{8}$.

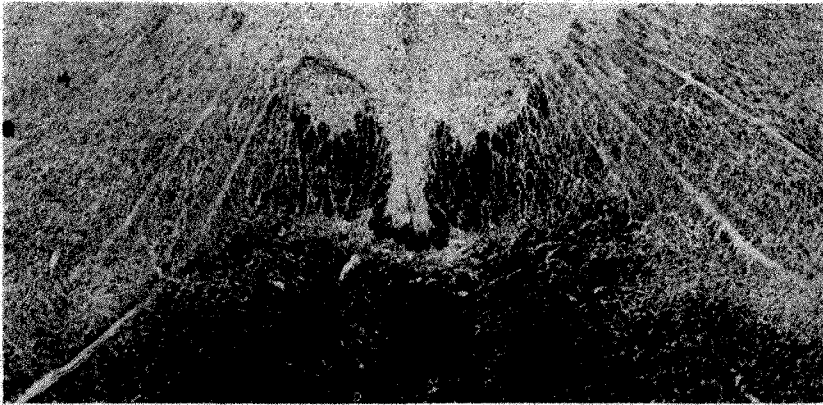


FIG. 2.—Normal fourth nerve nuclei for purposes of comparison with fig. 3.

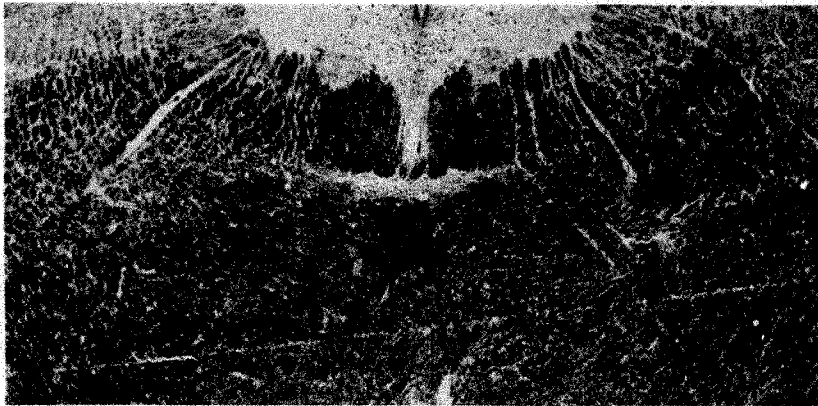


FIG. 3.—Showing pathological fourth nerve nuclei. The diameter of the nuclear groups appeared shorter than those of the normal nuclei of the control sections.

There was, therefore, very nearly complete loss of all extra-ocular muscular power, with preservation of the reactions of each pupil to light. Movements of convergence were practically impossible. The functions of the other cranial nerves were carefully tested and were found normal, as well as the muscles innervated by them. The muscular power of the upper limbs was entirely normal, and the biceps and triceps reflexes were normal. There was no

muscular atrophy. The muscular power of the lower limbs was equal and normal, the patellar and Achilles reflexes were normal, and the gait and station were natural. No additional evidence of disease could be discovered.

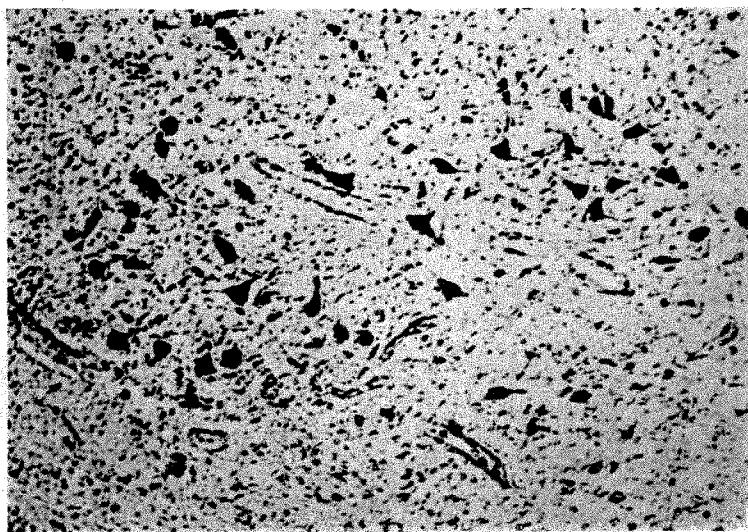


FIG. 4.—Cells of the sixth nerve nucleus from a normal case, for the purpose of comparison with fig. 5.

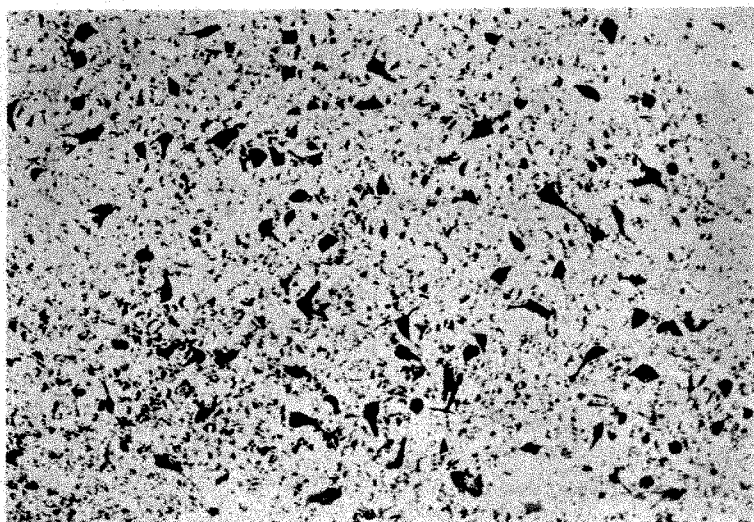


FIG. 5.—Cells of the pathological sixth nerve nucleus, showing the variations in size.

There was a moderate degree of general arterio-sclerosis, no greater, however, than might be expected in a normal woman aged 81.

The patient died of pneumonia at the age of 84 without having developed additional symptoms.

Necropsy report.—The sixth nerve nuclei were easily recognized. The cells of each nucleus were well stained, and chromatolysis was very slight when compared with the cells of a normal nucleus in sections made from a young adult for the purpose of control. The nerve cells were slightly diminished in number and presented definite variations in size and, to some extent, in shape. At least one-third or one-half their number were distinctly smaller in diameter than the others. Similar appearances were not observed in the control sections. The axis cylinders stained normally in Weigert sections. The bundles of fibres composing the root of the sixth nerves in their course through the pons appeared smaller in diameter and less numerous than those in the corresponding normal sections.

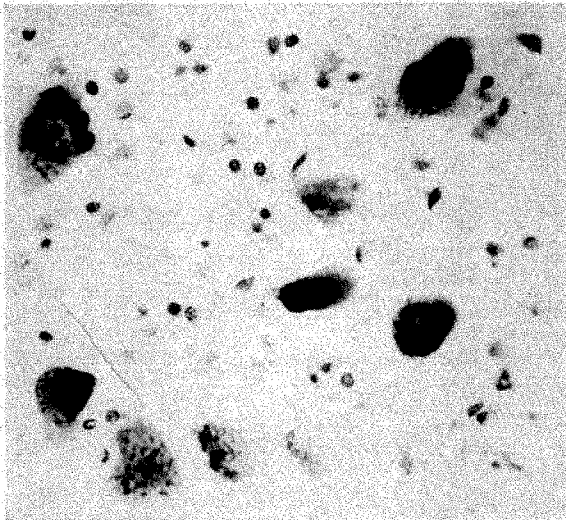


FIG. 6.—Cells of the oculomotor nucleus, one showing evidences of chromatolysis.

The cells of the trochlear nuclei presented the same appearances. The diameters of the whole nuclear groups appeared shorter than those of the normal nuclei of the control sections, and the bundles of the fourth nerve were smaller.

The cells of the oculo-motor nuclei of each side were slightly diminished in number, especially in the lateral cell groups in the sections of the middle and more caudal levels. In the sections from the more proximal levels, this diminution in number of cells was not so apparent. In no section, however, were the differences in the number of cells composing the different groups very striking, yet in the normal control sections the corresponding cells appeared more uniformly distributed and more numerous than in the pathological sections. Variations in the size of the cells were observed, but it was difficult

to determine whether these variations were much greater than similar differences in the size of the cells seen in normal specimens. Some cells had undergone chromatolysis, but this was not a conspicuous feature; many of the cells were deeply pigmented. The cells composing the nuclei of Darkschewitsch were normal in size and shape, and did not appear to be distinctly diminished in numbers, but contained much more pigment than was observed in cells of the oculo-motor group. The cells occupying the median position, corresponding to Perlia's nucleus, appeared normal.

The cells of the Edinger-Westphal nuclei were numerous, well-shaped, uniform in size, with clear nuclei and without chromatolysis, and were conspicuously free from pigmentation.

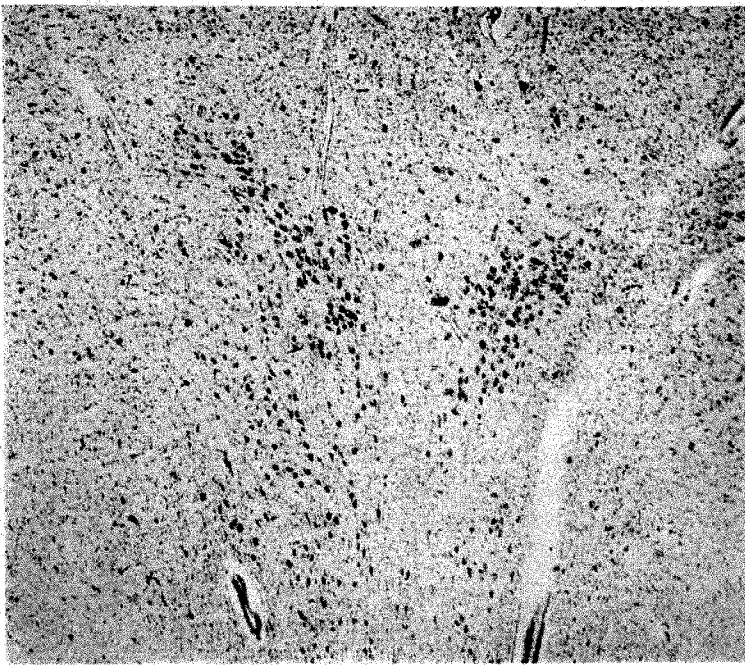


FIG. 7.—Showing preservation of the cells of the Edinger-Westphal nuclei.

The fibres of the oculo-motor nerves stained well by Weigert's method, but were much less conspicuous than in normal sections, and the bundles appeared smaller in diameter than normal. The internuclear nerve fibres (*fibræ rectæ*) were normal in appearance. There was no evidence of nerve degeneration elsewhere in any of the Weigert sections, nor was there any evidence of inflammatory reactions.

Sections of the third, fourth and sixth nerve trunks stained fairly well with acid fuchsin and Weigert's method, but these again appeared smaller in diameter than corresponding control specimens. The optic nerves were normal.

Comment.—We are fully aware of the fact that cells composing some nuclear groups may normally present variations in size. In the oculomotor nuclei differences in the size of the cells is well known, but pronounced differences in the size of the fourth and sixth nuclear cells are unusual and must be abnormal. According to most authorities, including Winkler [16], the cells of the fourth and sixth nuclei are more uniform in size than those of the third nuclei. Smallness of the ocular nerves was apparent, even to the naked eye, not only in their intramedullary course, but also the extramedullary nerve trunks. The other cranial nerves did not appear so small in comparison.

Senility does not produce distinct alterations in the size of the nerve cells, though Donaldson [6] has observed a shrinkage of the whole brain, determined by weighing, owing to old age alone. We know of no evidence that cessation of muscular contraction alone for a long period of time, as occurred in the extra-ocular muscles of this case, is capable of producing shrinkage of the nerve trunks innervating the muscles so affected, so we are forced to the conclusion that the alterations we have found were sufficient to explain even the extreme degree of ophthalmoplegia with which they were associated.

We wish to point out the striking resemblance of these changes to those found by Greenfield and Stern [8] and others in cases of progressive spinal muscular atrophy of childhood of the Werdnig-Hoffmann type, for we believe the case we have described must be regarded as a similar form of chronic neuron degeneration, though the alterations were entirely limited to the ocular neurons, and we think it is probably the same pathological process that produces progressive spinal muscular atrophy when the spinal neurons are affected. Why some of these cases of ophthalmoplegia seem to be hereditary or familial in character, as were Beaumont's cases, or develop sporadically in early and but seldom in later life, might be due to the same factors, whatever they may be, that determine the time and character of onset of the symptoms in spinal muscular atrophy.

The extra-ocular muscles were not examined, but had they been we are certain that they would have been found severely atrophied, for it is inconceivable that such severe neuron paralysis which had persisted for so many years would not have produced very decided muscular atrophy.

Collins examined a piece of excised muscle from his case and found it atrophic, but it was not examined microscopically.

Siemerling [13] reported a case of left-sided congenital ptosis, with

necropsy. The movements of the eyeballs were normal and the reflex pupillary movements were preserved. He found degeneration of the cells of the oculo-motor nucleus in the more proximal levels. The right oculo-motor nucleus was normal. He also stated that the intramedullary oculo-motor nerve bundles, as well as the fibres of the extramedullary oculo-motor nerve trunk on the affected side, were much thinner than normal.

Fuchs reported, in 1890, five cases which have already been referred to by Collins, in which bilateral ptosis was the only symptom of disease. In three of these the condition was acquired, and in two it was hereditary. The muscles of the eyelids were extremely wasted, and in a portion of these atrophic muscles excised for microscopical examination the fibres appeared much thinner than normal, the nuclei were increased in numbers and there was pigmentary degeneration inside the sarcolemma, but no fatty degeneration was found. The connective tissue between the muscle fibres was increased in amount. Fuchs discussed at length the difference in the appearance of muscles atrophic as the result of neuronie disease, and of that due to primary muscular atrophy, and emphasized that in the latter condition hypertrophy of some fibres is generally found. Though admitting that, in his case, because of the small microscopic specimens, differentiation was extremely difficult, he seemed to believe that it was in reality a primary myopathic disease.

Judging from Fuch's description, we think his cases of isolated ptosis must have been the result of primary myopathy, an entirely different disease from the case we have observed, and we have only referred to them for the purpose of emphasizing the important differences in the character of muscular atrophy. The muscles of the eyelids of Fuchs' cases were extremely wasted. In our patient the muscles of the eyelids were not atrophic, and obvious muscular atrophy has not been recorded in other cases of chronic progressive ophthalmoplegia that we have alluded to.

Implication of the extra-ocular muscles, exclusive of the levatores palpebræ, has rarely been observed in progressive muscular dystrophy (primary myopathy). Wilbrand and Saenger [15] refer to only two cases, one reported by Gowers, and one by Winkler and von der Weyde. Oppenheim [11] says that ocular paralysis has been observed very exceptionally in progressive muscular dystrophy, and refers to a few cases reported in the literature. Yuma Sunaga [17], in an article on the trophic innervation of the extra-ocular muscles in relation to experi-

mental and pathological studies on progressive muscular atrophy, says that he has had the opportunity of examining the eye muscles in two cases of progressive muscular dystrophy. Macroscopically, the external recti and obliques presented no alterations, but microscopically he found the characteristic picture of muscular dystrophy. After extirpation of the ciliary ganglion in dogs, he found alterations of the external eye muscles (recti and oblique) that resembled closely those of muscular dystrophy, and attributes these lesions to the cutting off of trophic innervation from the sympathetic nerves. He refers to the investigations of his colleague, Ken Kuré, and others.

Ptosis with paralysis of the extra-ocular muscles is well known in myasthenia gravis, a condition affecting striated muscles primarily, but the characteristic of this form of paralysis is the tendency to recover muscular function after rest, and rapid exhaustion of function from prolonged effort. Yet Collier [4] asserts that it is well known that the paralysis of myasthenia gravis may become complete and permanent. In our case there were no symptoms suggesting myasthenia gravis.

Spiller says [14], in discussing oculo-gyrations and the lesion causing complete bilateral ophthalmoplegia: "I believe that, when the central pathway of cortico-nuclear oculo-gyration is paralysed above or in the nucleus of the nerve to the affected internal rectus, the function of this muscle in convergence will disappear or become much impaired, as it did in the case I now report. When the break occurs in these fibres above this nucleus, no impulses can pass into this nucleus for either form of function of the internal rectus, i.e., for oculo-gyration or for convergence; but, when the break occurs in the posterior longitudinal bundle, and therefore below the nucleus of the nerve to the internal rectus, the function of the internal rectus muscle in convergence may be preserved, as it has no relation to the abducens nerve, but oculo-gyration demanding the function of this muscle in association with the function of the hetero-lateral external rectus will be lost. So far as I know, this diagnostic distinction of a lesion above the nucleus of the nerve to the internal rectus, as compared with one in the posterior longitudinal bundle below this nucleus as of value in localization, has not been described, and it applied to the lesion above the nucleus only when it is near the nucleus.

"Complete ophthalmoplegia, implicating all the nerves supplying the eyeballs, has been explained usually as the result of inflammatory lesions of all the ocular nuclei, but this explanation, when all other cranial nerves entirely escape, has seemed to me unsatisfactory,

especially as bilateral complete ophthalmoplegia has been repeatedly observed without other nerve lesions. I believe that when a lesion destroys the nuclei of the trochlearis and oculo-motorius nerves bilaterally, which a comparatively small lesion may readily do as these nuclei are very near together, it must destroy the connections in the posterior longitudinal bundles between the nuclei of the internal recti and those of the external recti, and consequently paralysis of the external recti muscles will result without any lesion of the abducens nerves or their nuclei. The movements of the two eyeballs are intimately associated, and a lesion of the central pathway of cortico-nuclear oculo-gyration near the nuclei affects the movements of both eyeballs."

Collier has described how a lesion situated above the oculo-motor nucleus is capable of producing complete ophthalmoplegia, but he points out that when ophthalmoplegia occurs from a lesion in this situation the eyelid is retracted and ptosis will not develop. In his case there was a hæmorrhage in the region of the posterior commissure, and retraction of the eyelid was observed. The oculo-motor nuclei were not implicated by the lesion; the paralysis, he thought, had been produced by destruction of the efferent ocular cerebral fibres in their course downward from the brain, before they had reached the level of the oculo-motor nuclei to connect with them.

In our case, and in all similar cases alluded to here, the pupillary reflexes to light especially, and to a less degree on accommodation, were preserved, and in our case the Edinger-Westphal nuclei were intact. This fact would appear to support the view so generally held that the function of the Edinger-Westphal nuclei is essentially for the control of the pupillary movements.

Brouwer has paid particular attention to this problem. He described a case of ophthalmoplegia in which the oculo-motor nerve had been compressed by an aneurysm of the carotid artery, but with the preservation of the pupillary reflexes, yet the cells of the Edinger-Westphal nucleus presented some alterations. He attributed the cell changes to retrograde effects of compression exerted upon the oculo-motor nerve. In discussing the literature of the subject, he referred to the cases of Cassirer, the work of Tschuda, Bernheimer, and others, and said he had been unable to find a single case recorded in the literature in which destruction of the Edinger-Westphal nucleus had occurred with preservation of the pupillary reflexes to light and on accommodation. From his studies of the literature and his own investigations in comparative and pathological anatomy, he concluded that the Edinger-Westphal

nucleus was certainly the sympathetic part of the oculo-motor nucleus, and referred to the fact that Jacobsohn had given it the name of "nucleus sympathicus nervi oculomotorii."

Wilbrand and Saenger, after having referred to the work of others, point out that the Edinger-Westphal nuclei lie so close to other cell groups of the oculo-motor nuclei that functional differentiation by experimental methods alone is exceedingly difficult. They quote the case of Gruenstein and Georgieff [9], in which there had been bilateral ophthalmoplegia with preservation of the pupillary reflexes. Microscopically, these authors found two lesions in the peduncles destroying most of the cells of the oculo-motor nuclei, while the Edinger-Westphal nuclei were preserved for the most part, only a very few of the cells in the posterior portion of one of the group were implicated in the lesion, which was a tubercle. They regarded this observation as important evidence that the Edinger-Westphal nucleus had to do with the pupillary reactions.

Leslie Paton and Ida Mann [12] studied the development of the third nerve nucleus in its bearing on the Argyll Robertson pupil, and concluded that the view that the median nucleus of Perlia is concerned with convergence, and the Edinger-Westphal nucleus with pupil movements, is supported by the study of their development in man, since the time of appearance of the various parts of the nucleus appears to be correlated with the development of the mechanism of their respective functions.

It is significant that Brouwer and Winkler both quote the work of Cajal, who said that although he had been able to demonstrate the Edinger-Westphal nucleus in the cat, mouse and dog by silver methods of staining, he had been unable to follow their axis cylinders into the oculo-motor nerve trunks, and consequently suspected it was not really part of the oculo-motor nucleus. It appears, therefore, that the cells of the Edinger-Westphal nucleus must represent a separate neuron system, and for that reason it was not affected in our case, thus explaining the preservation of the pupillary reflexes.

The most recent and most convincing work on the subject is that of Winkler. He says that the cells of the Edinger-Westphal nuclei do not send fibres to the oculo-motor nerve-roots, and consequently should not be considered as parts of the oculo-motor nuclei. By extirpation of the ciliary ganglion in cats, and also after section of the oculo-motor nerve, he found no effect whatsoever on the cells of the Edinger-Westphal nucleus. He points out that this result is diametrically opposed to Bernheimer's results, for Bernheimer believed he had been able to

establish that the Edinger-Westphal nucleus disappeared on the operated side after extirpation of the ciliary ganglion. Winkler thinks it probable that Bernheimer had been misled, because the Edinger-Westphal nucleus is inconstant and not easily recognized in some animals, and that he might have operated upon an animal in which, by chance, the nucleus was very poorly developed.

Winkler regards the Edinger-Westphal nuclei and also Darkschewitsch's nuclei as separate from the oculo-motor nuclei, and thinks they are intercalated groups of cells which have to do with the synergic movements of the eye, the latter representing part of the mechanism for the control of the upward, associated movements of the eyeballs. He describes the Edinger-Westphal nucleus as situated among the fibræ rectæ and surrounded by them, the fibræ rectæ passing through the grey matter between the proximal part of the main lateral groups of the oculo-motor cells. The Edinger-Westphal nucleus in the proximal levels forms an important intercalating apparatus and, with the nucleus of Perlia which is situated in the more caudal levels, receives innervations from the subcortical and, to a moderate degree, from the cortical regions. He thinks the Edinger-Westphal nuclei regulate all pupillary movements, not because they give origin to radicular sympathetic fibres, but because they receive a great number of fibræ rectæ.

We wish to thank Dr. William G. Spiller for his valuable assistance and suggestions in the preparation of this report.

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THE CEREBROSPINAL EPIDERMoids (CHOLESTEATOMATA).¹

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INTRODUCTION.

So many excellent papers have appeared lately on the subject of cholesteatomata of the brain that some explanation may be necessary for the appearance of another contribution. The first excuse lies in the relatively large number of cases which we have collected; moreover, we have been able to include a case of spinal cholesteatoma, which stands out as a particular rarity among a very uncommon class of tumours.

The present chaotic state of our knowledge as to the nature of these growths justifies an attempt at sifting the complicated evidence and placing the problems of histogenesis and pathology in a clearer perspective. Many of the contributions to this subject have done little to elucidate the complexities but have tended rather to obscure the issue, by complicating the terminology, by describing tumours of different types under the same name, or by giving different names to the same type of neoplasm. No less than nine distinct varieties of growth have at various times been spoken of as "cholesteatoma."

Roussy and Cornil [47] have indeed insisted on the fact that the term cholesteatoma cannot serve to define one variety of tumour; in their own words it can concern either inflammatory pseudo-tumours, or

¹ Work carried out at the National Hospital, Queen Square, London, under the auspices of the Medical Research Council.

tumours of the most diverse origin and nature which in the process of degeneration become laden with cholesterin.

Again, there has been much discussion in the past as to the histological type which these tumours represent; they are called epithelial by some, endothelial by others, while some authorities are unwilling to express any opinion as to their nature. The exact point of origin has again been in dispute; one school of thought, for example, attributes the neoplasia to an overgrowth of an inclusion of foetal cells; others look to the various components of the meninges as the source, and believe in an excessive growth of certain cell groups, which may or may not undergo metaplasia.

Lastly, the question of an uniform nomenclature is still a vexed problem. For reasons which will be given later, we shall adopt the term "epidermoid" as synonymous with that type of cerebral cholesteatoma exemplified by our personal cases.

HISTORICAL.

The story of the cholesteatomata has been told on many occasions. It is advisable, however, to review once again the chief milestones in the study of these tumours in order fully to appreciate the complexity and difficulties of the present situation. An exhaustive recapitulation of the literature is not necessary and it will suffice to recall in brief the outstanding contributions to the subject.

Verattus [58], 1745, is usually quoted as being the first to record one of these tumours, but the possibility that it was a teratomatous type of growth and not a hair-containing cholesteatoma cannot be overlooked. His patient, a woman aged 40, whose health had hitherto been uneventful, sustained a sudden ictus; on the third day she became febrile; the following day her temperature was higher, and she died on the fifth day of her illness. Autopsy examination revealed a brain tumour containing masses of hair. There were no bulbous roots to the hairs, both ends of which tapered. Verattus remarked upon the occasional occurrence of hair-containing tumours in other parts of the body, but stated that the presence of such growths within the brain must be extremely rare; he was at a loss to explain their origin within the cerebrum, since fatty tissue did not occur here.

Duméril [13], in 1807, exhibited some pathological wax models before the Société de Médecine, including one of a brain tumour. This was white and silvery on the outside with a greyish-white interior and grew in the cerebellum, apparently from the fourth ventricle. No

clinical notes were available, but Cruveilhier, who quoted this case twenty years later, stated that it had occurred in Dupuytren's service at the Hôtel Dieu in the period 1803-1804. Dupuytren himself confessed ignorance when questioned about the case.

Le Prestre [29], 1828, described under the title of *tumeur adipociriforme* a growth lying in the median excavation of the brain, growing backwards to the left, compressing the pons, medulla and cord. The author described the macroscopic appearance in the following words: "Mamelonnée, dont les granulations sont en tout semblables à des perles, l'aspect aussi brillant que l'intérieur de certaines coquilles. Coupée dans son milieu, elle paraît formée de couches concentriques, unies entre elles par des laines de tissu cellulaire. On n'y observe aucune trace de vaisseaux; sa couleur est d'un blanc opaque, sa densité plus considérable que celle du cerveau." Full clinical particulars were given.

In the following year appeared the work of Cruveilhier [11], to whom we owe the earliest complete description of a specimen and the first commentary as to its nature and source of origin. To him also we owe the term "tumeur perlée." In his case, a growth was found at the base of the brain distorting in an upward direction the vault of the third ventricle and the corpus callosum; it filled the median excavation and advanced as far forwards as the pituitary, distending the optic commissure. The exterior of the growth was of a "metallic sheen like silver or like a pearl of the finest water." It was covered by adherent arachnoid and on cross-section it revealed a yellow-white interior of the consistency of soft wax. According to Cruveilhier, the tumour was a product of secretion which had obviously originated in the serous subarachnoid cellular tissue. No histological description was given, but a chemical analysis was made by Bannel with the following result: "The crystalline nacreous material presented all the characters of cholesterin; the concretionary material approximated closely in nature to stearin."

In 1834, Peyrot [43] reported the case of a mirror-maker, a sufferer from chronic hydrargyria, who died suddenly at the age of 36 from an hæmoptysis. Post-mortem examination of the brain revealed at the posterior end of the pons a tumour, the size of a small nut—"formée par des paillettes nacrées, et tout à fait semblable à celles déjà décrites dans l'ouvrage de M. Cruveilhier." This neoplasm, which was adherent to the cerebellum, was covered by arachnoid.

Five years later appeared a record of two cases of "geschichtete.

perlmutterglänzende Fettgeschwülste" by Müller [38], who first employed the term "cholesteatoma."

Adams, in 1851 [1], gave the first description in this country of one of these tumours, and he also furnished a good histological account. In his case the tumour, which lay beside the pons, was described as having a mammillated surface, smooth, translucent and pearly. Microscopic section revealed a thin membranous layer "like tessellated epithelium." In the interior the cells were extremely pale and delicate, irregular in outline and were mostly without nuclei. Here and there were plates of cholesterin. Adams compares his tumours with those of Müller's.

Three years later appeared von Remak's paper, in which for the first time we find the suggestion that these tumours may have arisen from misplaced epithelial tissue (" . . . die vielleicht schon auf einer frühen embryonischen Entwicklungstrife").

In 1855, Virchow [59] described a number of cases of cholesteatoma, some of them visceral and others intracerebral; in two cases the tumour arose within the substance of the temporal bone. Virchow suggested the term "margaritoma," but adopted in the main Cruveilhier's expression, and spoke of them as "Perlgeschwülste."

The first case of cerebral cholesteatoma, which was operated upon, was described in 1856 by Esmarch. The tumour in this case appears to have grown from the cranial vault in the frontal region. Numerous other examples were then recorded—mostly either in the nature of isolated case reports or else mentioned in discussions upon cerebral tumours in general. Thus, in this country we had the cases recorded by Peacock [41], Wilks [61], Price, Knowles. In France we had the cases of Spillmann and Schmidt, and in later years Parent-Duchateler and Martinet, and Marie and Roussy. Most of the cases, however, were recorded in Germany, as by Ladame, Bernardt, Petrina, Eberth, Mayer [37] and Foerster. To Eppinger [1875]¹ belongs the credit of being the first to record an instance of a cholesteatoma growing within the spinal canal.

The literature now becomes more critical and the questions of origin and histological identity come up for discussion. Perls [42], in 1877, was the first to cavil at the accepted conclusions of his time, and he suggested that the cholesteatomata were of endothelial origin. He further specified the endothelium of the neural lymph spaces as the

¹ Eppinger, *Prag. Vierteljahrschrift*, 1875, quoted by C. Frank.

site of origin. In this view he was supported by Frank, Schmaus and Nehr Korn. Beneke, too, supported this view, but altered his opinion later.

In 1897 appeared Bostroem's [9] masterly and meticulous work on the intracranial cholesteatomata, lipomata and dermoids. He reviewed all the cases hitherto recorded, numbering thirty-two in all, and added two others of his own. Full pathological investigations were made, and Bostroem leant strongly to the view of an epithelial origin. He suggested the title "*piale epidermoïde*," and stated that they arose from embryonic skin elements at a comparatively late stage; he brought them into line with the pial dermoids, which arose from epiblast of an early embryonic type, and later produced both epithelial and connective tissue elements.

A contribution to the problem now came from America, where Blumer [8] (1900) made an excellent summing-up of the situation as it existed at that time. He added a personal case which proved microscopically to be of endothelial type; the epithelial nature of the typical cholesteatoma seemed to him beyond question, so he tentatively postulated the existence of two or more varieties of tumour, the one epithelial, and the other endothelial, his own case belonging to the second group. Blumer furthermore pointed out the similarity in structure between his specimen and the so-called cholesteatomata of the lateral ventricles found in horses.

No important contribution—other than a few isolated case reports—appeared for the next twenty years, until the publication of Bailey's paper [2] in 1920. Bailey rediscussed the problem with admirable clearness, and added two personal cases: from a study of the literature he estimated that sixty-two cases of cholesteatomata had been recorded up to date. He gave a pathological description and considered the tumour as being composed of four concentric layers. Although inclined to favour the theory of epithelial origin, he regarded the exact site of origin as uncertain. For this reason he rejected Bostroem's title of pial epidermoid and reverted to the expression "pearly tumour."

In 1922, Horrax [20] reported three more cases, some of which contained hair. He again brought them into line with dermoid tumours, which he believed differed only in the degree of inclusion of the original dermal layer. Horrax preferred the term "cholestatoma" which he qualified by prefixing "meningeal."

The same year Cushing [12] recorded the case of an "epidermal cholesteatoma" growing within the skull bones, and he collected from the literature some ten other similar cases.

Bailey's second paper [3] appeared in 1924, and in it further cases were added to the literature.

The last noteworthy contribution appeared in 1925, when Kakeshita [23] dealt with the pathology of two specimens belonging to the Neurological Institute of Vienna. This paper is of interest in that the author appears as a modern exponent of the theory of endothelial origin.

PATHOLOGY.

The naked-eye appearance of these tumours is in most instances so constant and characteristic as to render possible a correct pathological diagnosis at sight. According to the site of growth and length of history, the size varies, but as a rule the tumours are of some magnitude at the time of operation or at autopsy. Thus, the tumour may attain the size of a large orange, and weigh as much as 70 grm., as in Kay and Pack's [25] case. They are usually ovoid or spheroidal in shape; the surface is not uniform but is irregularly lobulated (*mamelonné*). The most characteristic feature, however, lies in the well-known appearance of the capsule, which is opaque, white and glistening. So striking is this appearance that it never fails to cause comment and has impressed every observer. At various times the capsule has been compared with silver or with the interior of a shell. The commonest term, however, is that of "pearly tumour," an expression originally employed by Cruveilhier and still in use by many.

Although this pearly exterior is so outstanding a feature at operation, the sheen tends to become dull and finally disappears when the tumour has been preserved in formalin. Museum specimens, therefore, seem disappointing when compared with the appearance or descriptions of the tumour *in vivo*. In certain cases (Case 3) this nacreous capsule is surrounded by a fibrous capsule which loosely envelops the tumour. This is by no means constant, however, and was absent from the majority of our cases. Sometimes, in the fresh specimens, glistening crystals of cholesterin may be seen adhering to the surface of the tumour.

The adjacent brain tissues are usually in no way infiltrated by the neoplasm but are sharply demarcated. With tumours of large size some degree of compression is inevitable. In those rare instances in which the tumours appear to grow within the substance of the brain, Benda [4] has shown that there is an actual invasion and destruction of nerve-tissue. A more or less intimate association with the pia-arachnoid and a definite point of attachment is demonstrable in most of the cases.

The cholesteatomata are firm but brittle on palpation, and possess none of the hardness of some of the endotheliomata and fibromata. The capsule is apt to separate from the bulk of the tumour with the slightest roughness of handling and the rest of the neoplasm then tends to fragment. True cystic degeneration is not seen, but in old-standing growths the interior caseates and undergoes necrotic change, giving rise to a sensation of "yielding" to the finger.

The cross-section also presents a characteristic appearance. The cut surface is usually uniform in consistency from without inwards; it is composed of finely granular material, sometimes showing a flaky or laminated tendency. At various times the tumour on cross section has been compared with sago, marzipan or cocoanut icing. Müller used the expression . . . "zerworfener Felsmassen von geschichteter Bildung." In the fresh specimen the colour varies from white to cream or pale yellow; after preservation in formalin the colour becomes less vivid. If the cross-section is made in another plane the growth is seen to be composed of concentric laminae and the appearance is not unlike that of an onion. The actual surface on cross-section may give a characteristic soapy or waxy feel to the finger, and the greasy nature of the tumour is frequently betrayed by its effect upon the knife. Some writers have drawn attention to a peculiarly fatty and distinctive odour given off by the growth when cut across.

In some of the recorded cases (although not in any of our present series) hairs have been visible. As a rule they are few in number and appear to grow from the capsule and to extend inwards into the main mass of the tumour. At the point of attachment to the pia the hairs tend to be most numerous.

A noteworthy feature of the epidermoids is the rarity or absence of blood-vessels.

It is obvious from a consideration of the recorded cases that there are particular sites of election for the growth of these tumours. Most of the epidermoids arise from the subarachnoid cisterns. Those which are most anterior in their site of origin tend to fill the cisterna interpeduncularis, and by upward extension they may come into close relationship with the third ventricle. In some instances the epidermoid seems to arise from the apex of the invagination of the pia-arachnoid which forms the velum interpositum and pushes forwards the posterior wall of the third ventricle. A very common site is below the tentorium cerebelli. Here they grow in one of two chief situations; they may fill the whole of the lateral recess and become closely associated with the

peripheral course of the fifth, seventh and eighth nerves, or they may appear on the ventral aspect of the cerebellum, lying strictly in the middle line. In the latter case the site of origin is apparently at a point within the fourth ventricle, and a longitudinal section through the vermis reveals the cavity of the ventricle distended and entirely filled with neoplastic tissue. A few cases of epidermoid tumour are encountered in situations remote from those just mentioned. Thus, in a few recorded instances, a tumour has been described lying within the substance of the

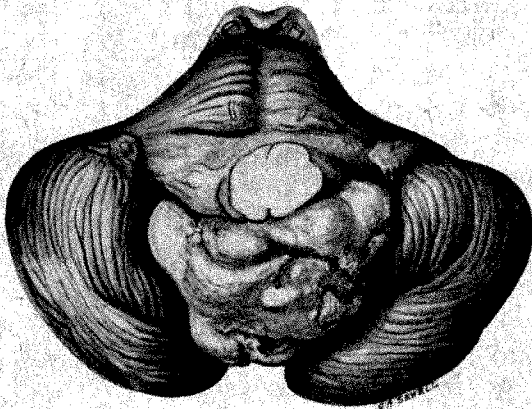


FIG. 1.—Epidermoid of the fourth ventricle (from the Museum of the R.C.S. 1459. 1). The patient, a woman aged 30, was admitted to hospital with a three weeks history of occipital pains, inability to walk, and dysesthesia in the hands. She was dull, tremulous and dysarthric; gait ataxic; knee-jerks exaggerated; defective muscle sense in arms. (See KNOWLES, *Lancet*, 1902, i, 1833.)

hemisphere (cf. Cases 7 and 8). The temporal lobe is then the most usual region; under favourable circumstances it is generally possible to demonstrate a more or less delicate connection between the growth and the leptomeninges of the base.

The histology of these tumours is remarkably constant in appearance and arrangement. Variations do occur, however, between individual

specimens, but only in minor particulars, and the variability mainly concerns the proportionate distribution of one constituent compared with another. In the earlier recorded cases the microscopic descriptions are strikingly uniform, and the nature of the growth is quite clear from the accurate reports.

Cruveilhier did not furnish any histological details in his original paper, although he gave the results of chemical analysis. We owe the first account in this country of the microscopical appearance to Adams; he spoke of a thin membranous layer "like tessellated epithelium"; the cells were described as being extremely pale and delicate and generally without nuclei; they had irregular sides. Plates of cholesterin were visible in the substance of the tumour. Later descriptions emphasized the peculiar structure of the capsule, which we learn was composed of flattened epithelial-like cells, resembling in appearance and in staining properties the cell elements of the skin (Virchow, Benda, Bostroem and others).

Following the precedent of Percival Bailey, one usually considers the epidermoids as being made up of four concentric layers of different thickness, named, from without inwards, the stratum durum, the stratum granulosum, the stratum fibrosum and the stratum cellulosum. Each of these layers is liable to become detached and to lie free. As a result, the epidermoids are difficult to fix and cut satisfactorily, and the microscopic picture is usually fragmentary and ragged.

Most externally lies the stratum durum, which is variable in thickness in different specimens. This is the layer which is responsible for the typical nacreous sheen. In some instances, as in Marie and Roussy's case and our Case 3, it may be so thick as to constitute a tough fibrous envelope. It readily becomes stripped off, so that it is usually seen as a laminated mass lying independently of the stratum granulosum. Layers of collagen fibres, with little or no trace of cellular formation, constitute the minute structure. The individual fibres are loosely packed and when seen longitudinally are wavy in outline. In the deeper parts immediately overlying the stratum granulosum there may be a tendency towards densification. Occasionally in these deeper layers oval cells are seen with their long axes lying horizontally; the nature of these is doubtful, but some of them resemble plasma cells.

Beneath the stratum durum lies the characteristic layer which constitutes the histological criterion of the epidermoids. The stratum granulosum, as it is called, is essentially a cellular layer which stands out in vivid contrast with the rest of the tumour both in appearance

and in staining properties. As a rule there is a narrow interval which separates the stratum durum from the stratum granulosum. The depth of the granular layer varies with the specimen; in some instances (e.g., Case 2) it is only one or two cells in thickness; in others (e.g., Case 9) it may be built up of ten or more layers of cells which vary in character according to their depth. This layer stains intensely blue with iron hæmatoxylin, which is not only taken up by the nucleus and all its granules but also by the cytoplasm itself. The typical cell is a comparatively large, oval or circular structure with a large rounded nucleus. The cells are not packed tightly together, but clear intercellular channels separate one from another. It is occasionally possible,

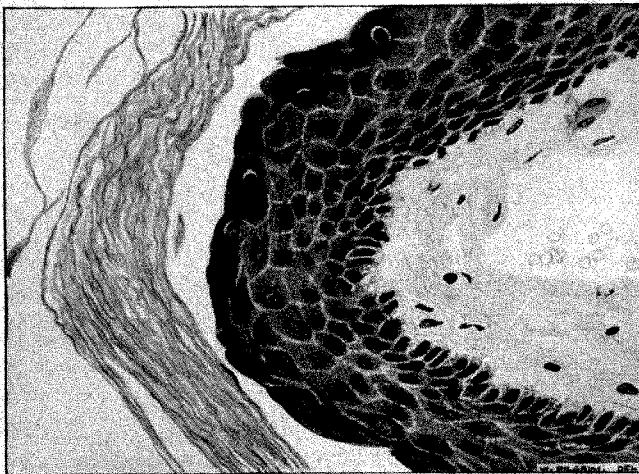


FIG. 2.—Section of tumour from *Case 9*. Here there is a very wide epithelial layer composed of several rows of cells with an arrangement and appearance which alters in the characteristic fashion according to the depth.

as in *Case 9*, to demonstrate intercellular bridges surmounting these moat-like spaces and connecting adjacent cells. Benda was the first to describe these bridges, and other observers have at times succeeded in demonstrating them; in most specimens, however, they are not visible. Fine granules, composed of keratohyalin, are scattered throughout the cytoplasm. The chemical nature of these granules is identified by their staining reactions with Heidenhain's iron hæmatoxylin, Delafield's alum hæmatoxylin and with Kresyllichtviolett. In the deeper layers of the stratum granulosum the granules become larger and more numerous.

The morphological characters of the component cells vary according to their depth. Immediately below the stratum durum the cells are oval and are arranged tangentially to those in the overlying layer. A palisade formation may therefore result, provided that the section is cut in an accurate transverse direction. Granules are less easily seen here partly because the nucleus stains intensely dark and occupies almost the whole of the cytoplasm. Below this layer is an intermediate zone of rounded cells; the apposition of one cell to another is loosest here and the intercellular channels are clearly seen. There appears to be no definite cell arrangement. In the deepest layers the cells are more oval and are arranged with their long axes parallel with the stratum

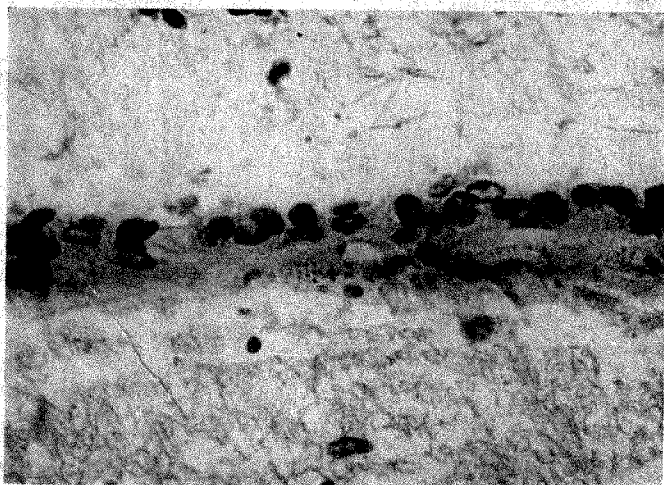


Fig. 3. — Microphotograph of the epithelial layer of Case 4, showing granules of keratohyalin (haematoxylin and van Gieson preparation).

durum. The nucleus stains less darkly and does not completely fill the cell; granules are here very numerous.

Here and there the stratum granulosum appears to send papillary processes into the more superficial stratum durum; in such places this particular stratum is thicker and may comprise six to ten cell layers.

The majority of tumours, however, possess a comparatively thin stratum granulosum, which shows no evidence of a papillary formation. In such a case the stratum consists of a superficial layer of large swollen cells, polygonal in outline, with pale, oval and faintly staining nuclei, and a granular cytoplasm; between the component cells are definite clear channels. An indeterminate layer occupies the central area and

is made up of a structure in which the outlines of horizontally flattened cells are barely visible. Deepest of all comes a single layer of ill-defined cells bearing numerous pigment granules.

There is usually a sharp line of demarcation between the stratum granulosum and the deeper layers of the tumour; frequently there is an actual gap between the two zones. Bailey speaks of a stratum fibrosum and of a stratum cellulosum as comprising the innermost zones of the neoplasm. These terms are not entirely satisfactory, however; a clear differentiation into two strata has not in our experience been possible; the tissue which immediately underlies the stratum granulosum seems

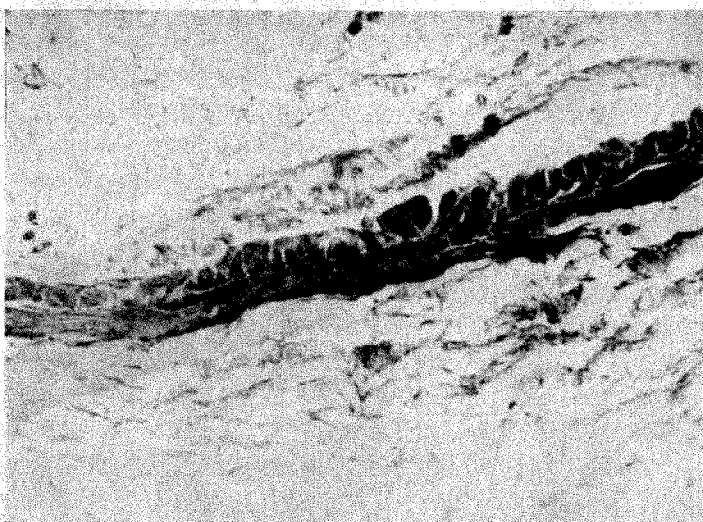


FIG. 4.—Microphotograph through the stratum granulosum of *Case 7*. The appearance is typical of the narrow type of epithelial layer. (Hæmatoxylin and eosin preparation.)

to pass by a gradual transition into the main central mass of the epidermoid. The superficial appearance of the layers deep to the stratum granulosum bears some resemblance to the stratum durum; it is made up of loosely packed layers of wavy homogeneous laminæ with the staining properties of keratohyalin. No stray cells are seen in this zone. The laminæ appear somewhat like fibrous tissue, but differ in their staining properties; they do not stain by van Gieson's method, and in aniline blue-orange-G preparations they are coloured quite differently from fibrous tissue and appear usually as a yellowish structure.

The interior of the neoplasm is made up of similar laminated tissue, arranged in a very loose mesh. In places, the cell outlines are

visible but no nuclei are seen. The fresh specimens show in this area numerous flat cholesterin crystals, but in the process of fixing and dehydration the cholesterin becomes dissolved out. Nehrkorn compared the structure of this zone with the histological appearance of plant tissue; for this reason Bailey proposed the name *stratum cellulosum*. This term, however, is apt to suggest a cellular type of structure and the original botanical significance may be overlooked. Perhaps a more appropriate name for the tissue constituting the bulk of the tumour would be *area cornea*, as implying a similarity in appearance and chemical properties with the most superficial elements of the dermis.

Throughout the whole of the tumour blood-vessels are not seen and there is an absence of vascularity.

It is clear from the description of these tumours that we are dealing with an epithelial neoplasm. The essential layer is the so-called *stratum granulosum*, which is obviously composed of epithelium varying from stratified to cubical in character. Mesoblastic tissues, where present, serve merely as supporting structures. The nature of these tumours can be best understood by regarding them as epidermal in character. The cholesteatoma is made up of an external epithelial membrane, outside which is a delicate fibrous tissue envelope. The interior of the tumour is composed of the accumulated products of the desquamated epithelial layer. In other words the *stratum granulosum* corresponds with the dermis and the *area cornea* with the *stratum corneum* of the skin and a *débris* of cast-off dead and horny scales.

Examining this premise more closely, the epithelial layer of the cholesteatomata apparently corresponds with several layers of the dermis. Most superficially we have the *rete mucosum* with its large loosely packed pale prickle-cells and clear intercellular channels; in the most external layer of all the cells are arranged in a fashion recalling a palisade appearance. Most internally is a layer of flattened pigment-laden cells, which is obviously analogous to the *stratum granulosum* of the skin. The homologue of the *stratum lucidum* is in places suggested by a narrow layer of indistinct, pale cells lying between the *stratum granulosum* and Bailey's *stratum fibrosum*.

In the *area cornea* we obviously have the retention products of shed horny squames, which are in the most part without nuclei. The presence of cholesterin crystals in this zone is explained by the breakdown of keratin and keratohyalin.

Support is given to this theory of the epithelial and epidermoid

origin of these tumours by the not infrequent finding of hairs within the neoplasm. Originating in the epithelial layer, they usually grow inwards so as to project into the mass of the tumour. The question of the occurrence of other specialized epithelial structures, such as nails and teeth in the cholesteatomata, will be discussed later, when the association of the dermoid and epidermoid tumours is dealt with. The presence of these and other structures of mesoblastic origin will obviously depend upon the depth of the original epithelial anlage.

Despite these striking arguments suggesting that these tumours are of epithelial nature, certain writers, as we have seen, regard them as endothelial. The argument has been reopened in recent years by Kakeshita, who, as we shall see, described the histological details of two cases and regarded them as cholesteo-endotheliomata. The story of this discussion may be briefly outlined.

Von Remak's hypothesis as to the epithelial nature and origin of these tumours remained unchallenged for many years. In 1877, however, in his textbook of pathology, Perls made the unconventional statement that "with reference to the cholesteatomata of the cerebral envelopes, it is very probable that one is dealing with an overgrowth of the endothelium of the perivascular lymph spaces; hence they are pure endotheliomata." He admits the existence, however, of transitional hair-containing forms suggesting an epithelial influence, and brings them into line with the dermoids. Other German lexicographers followed this opinion; Klebs [26], for example (1889), agreed that these growths were endothelial in type. Schmaus (1895) [49] too subscribed to this viewpoint. Glaeser 1890 [16] believed that the cholesteatomata arose from proliferation of the subarachnoid epithelial cells, as a result of some unknown stimulus. At first the growth occurs in scattered islets, but later the connective tissue atrophies and the isolated masses then run together. As the result of pressure the growing cells become flattened so as to form scales. Although it was admitted that epithelium is found in those places which are common sites for the cholesteatomata, Glaeser still thought that they were endothelial. He quoted Virchow's views of the metaplasia of tumours and referred to Koster's work on the growth of epithelial cancer from the endothelium of the lymphatics. The author summarized his views in the statement that these tumours resembled epithelial cancer, but they undoubtedly arose from the middle germ layer (". . . "zweifellos von Abkömmlingen des mittleren Keimblattes stammen").

In his earlier publications Beneke [5] also favoured the idea of an

endothelial character of these growths; he thought that the cholesteatoma cells, when subjected to a process of silver impregnation, conformed to the endothelial type by reason of the sharpness and regularity of their outlines. Benda, however, demonstrated equally clear-cut cell outlines in silver preparations of known epithelial growths, arising from the cornea. At a later date Beneke became converted to the epithelial school.

In 1897, Nehr Korn [40] recorded a case of a cholesteatoma occurring in a man aged 44, who had shown little physical disability during life, but had altered mentally so that the diagnosis of general paralysis was made. At the autopsy two mother-of-pearl tumours were found; one, a diffuse, broken mass, lying in the region of the pons and upper medulla, compressing the brain and burying the sixth, seventh, eighth, ninth, and tenth cranial nerves on the left side. The second tumour lay enclosed within the substance of the left temporal and occipital lobes, but was connected with the basal meninges in one place. Nehr Korn was unable to demonstrate either keratohyalin or intercellular bridges, and from the reaction of the tissues to various stains, particularly thionin and silver, he concluded that the tumour was of endothelial nature, "in the form of an endothelial pearl tumour."

Blumer's detailed report of a case of cholesteatoma—which is referred to in more detail later on—is a further contribution to the endothelial conception.

But the possibility at once arises as to whether these authors who subscribed to the endothelial theory were actually describing the same type of tumour. It is conceivable indeed that there may be at least two types of growth, superficially of cholesteatomatous nature, but differing in origin. Such a hypothesis seems to be supported by subsequent work.

Thoma [54], for example, takes up a somewhat similar attitude; while apparently advocating the epithelial origin of the cholesteatoma, he also states that tumours of exactly the same structure are found in the leptomeninges, where they apparently arise from the endothelial cells which line the trabeculae of the arachnoid.

In the later (1910) edition of his *Lehrbuch*, Schmaus, who it will be remembered was originally an exponent of the endothelial theory, now takes up the view that there are at least two distinct types of cholesteatoma, one consisting of flattened cells, epithelial in origin, and the other which comes into the category of endotheliomata.

Amongst later writers, Bland-Sutton [7], too, inclines towards the

view of an endothelial origin of the cholesteatoma, and tends to use the terms psammoma, endothelioma and cholesteatoma synonymously.

The hypothesis of the endothelial origin of the cholesteatomata has received a further impetus in recent years by the work of Kakeshita. This author (1925) examined with minute care two museum specimens from the Vienna Neurological Institute. The first was a pearly tumour measuring $5.6 \times 3.7 \times 4.8$ cm. lying within the substance of the right temporal lobe; a very definite connection with the basal meninges was, however, apparent. Histologically, the tumour was composed of cells of an endothelial type, which in places became degenerated and elongated in form and in such places took on the superficial appearances of epithelial cells. These were arranged in two or three layers with an almost palisade-like formation. Most peripherally the cells were cuboidal or polygonal, and contained a distinct nucleus. Towards the interior the cells were larger and the nuclei resembled in many respects those of typical epithelial cells. There were no intercellular bridges and no keratohyalin granules. Lipoid was present in most of the cells. The author insists that the cells contained in the tumour walls were typically those of a dural or arachnoidal endothelioma.

His second case was of a tumour the size of a walnut, lying in the fourth ventricle. The external appearances were those of a typical cholesteatoma, and there was a distinct connection with the meninges. The wall of the tumour consisted of a connective tissue meshwork containing round cells in which lay depositions of some homogeneous material. There were two distinct parts to the tumour, one of which was typically endotheliomatous; the other portion contained horny elements. Kakeshita would not allow of a chance juxtaposition of two different types of tissue, as he could trace every type of transition element from one to the other. He concluded that some at least of the so-called cholesteatomata were endothelial in character, and he thought that such neoplasms probably constituted a class of growth which could be termed cholesteato-endotheliomata.

From a study of the photomicrographs which accompany his paper, we cannot see any structures which resemble in any way the tumours in our present series. Kakeshita's cases—judging both from his description and from his illustrations—appear to be examples of an entirely distinct type of growth.

Despite the view of Klebs, Perls, Nehr Korn, and Kakeshita, we cannot subscribe to any hypothesis as to the nature of these tumours other than the epithelial; from an histological study the impression is gained

of an essentially epithelial type of growth. The layer of flattened cells which bears so close a resemblance to stratified epithelium, the interior formed of the aggregation of desquamated scales and their breakdown products; the positive finding of keratohyalin within the tumours; the occasional presence of hairs, all confirm the conception of an epithelial growth. Nor is there any unequivocal evidence which can be quoted to the contrary. The most obvious probability is, of course, that there is more than one type of tumour described as cholesteatoma, the most usual variety—of which our cases are examples—being clearly epithelial; while the other group, of which Klebs and others have written, are definitely endothelial. Of this latter class, we have had no personal experience.

The presence of an heterologous epithelial type of growth, lying in close apposition to the brain and associated more or less closely with the meninges, obviously requires explanation. Two main possibilities assert themselves: as Martin, Dechaume and Puig [36] have stated, the question is whether the epidermoids arise from foetal inclusion of epithelial cells, or whether they result from metaplasia of the endothelial cells of the meninges.

Virchow was perhaps the first exponent of the metaplasia school. Basing his argument (fallaciously, as we now know) upon the cell clusters occurring in the cancrioid, he attributed the growth of cholesteatomata to a metaplasia of similar clusters (Zellzapfen) lying within the layers of the arachnoid. He stated that these cells may be seen exhibiting all stages of cholesteatoma formation, cornification, desquamation of horny elements and cyst formation.

Eberth, and later Glaeser, also favoured the view of metaplasia of the endothelium and perithelium of the arachnoid spaces. Benda also subscribed to a metaplasia hypothesis, but believed that the primary tissue comprised the cells lining the embryonic medullary tube; he tentatively hazarded the possibility that diverticula from the cerebral ventricles might have constituted the starting point of the cholesteatomata (" . . . und mit dieser zusammenzuhängen scheinen, aber durch ihre regelmässigen kubischen Zellen weniger wuchernden Cholesteatomzapfen als kleinen Divertikeln der Ventricelwand gleichen.")

If the metaplasia theory were correct one would expect to find transition forms between epithelial and endothelial elements occurring in the same tumour; such has not been our experience. Nor can one readily point to any external factor—mechanical or chemical—respon-

sible for transforming one type of cell into another totally distinct variety. The causes of metaplastic tumour formation elsewhere are usually obvious.

We are inclined to favour the view that these tumours are essentially and primarily epithelial, and that they arise not by a process of metaplasia of normal cell structures, but from the overgrowth of epithelial rudiments. We assume a foetal inclusion of epidermal cells which, according to the depths of the layer or according to its embryonic antiquity, will produce either an epidermoid or a dermoid type of tumour.

The sites of election of the epidermoids have already been discussed; the problem now presents itself as to the possibility of correlating our clinico-anatomical facts with the conception of an epithelial rudiment.

It is tempting to conceive of an inclusion of epithelial cells occurring at the time of the formation of the foetal flexures. Thus, if at the pontine flexure a few epidermal elements became cut off from the exterior, they would remain in the region of the lateral recess as a potential anlage. In such a manner one might explain the growth of epidermoids in the regions of the cisterna basalis, the ponto-cerebellar angle and the fourth ventricle. A similar cutting off of cells in the region of the cephalic flexure would account for the more anterior cholesteatomata growing in the region of the third ventricle. This viewpoint coincides with that of Scholtz [50], who dates the origin of cholesteatomata from the time of the closure of the medullary tube or of the mouth flexure (third to fifth week).

In this way an adequate explanation can be offered for the occurrence of the majority of the epidermoids, that is to say, those arising from the basal excavation of the brain. The origin of the intracerebral tumours, the intradiploic and the cholesteatomatous growths within the spinal canal will obviously still require elucidation. There is no evident reason why the same factor of epithelial cell inclusion cannot be cited; indeed, our eighth case seems to lend weight to this idea. The erosion of the skull bones, obviously from a without-within direction, and the presence of paired and identical tumour formations connected through a narrow foramen, suggest that the scalp tumour was the primary one and had later spread into the cranial cavity.

Benda's theory of an origin from the embryonic medullary tube clearly fails to explain all the data; it cannot account for the occurrence of epidermoids completely unassociated with the ventricles; it does not easily explain the occurrence of neoplasms lying outside the strict midline of the brain or cord.

In the light of the work of Harvey and Burr [19] on the development of the meninges, the explanation of the occurrence of epithelial elements in association with the membranes becomes intelligible. These authors showed that the view of His and Kölliker—that the pachymeninx and the leptomeninx have a common origin, a primitive mesenchyme derived from a specific germ layer (the mesoderm), is incorrect. They proved, on the contrary, that certain ectodermal elements, derived in large part from the neural crest, are contributed to the mesenchyme and take part in the formation of the leptomeninx.

It now becomes necessary to consider some of the other varieties of tumour which have been spoken of by various authors as "cholesteatomata." Within this category will be included certain of the suprapituitary cysts; the teratomata of the brain; the endothelial type of cholesteatomata; the epithelial masses associated with chronic ear disease; the so-called cholesteatoma of the ventricles as met with in the horse, and lastly the pearly tumours of the cranial bones.

"Cholesteatomatous tumours" (of Rathke's pouch).—Before discussing the nature of the intracranial cholesteatomata, it is necessary at the outset to exclude definitely many of the cholesterol-containing juxta-pituitary cysts. The term cholesteatoma has in the past been loosely and inaccurately applied to certain of the epithelial tumours arising from unobliterated portions of Rathke's pouch. Such tumours readily break down to form cysts in which cholesterol is a prominent constituent. Many of these tumours, which have been confused with the cholesteatomata, are true adamantinomata. In others, e.g., Lockwood's case [30], the exact nature of the tumour—although almost certainly epithelial—is less clear. It cannot be emphasized too strongly that the presence of cholesterol within a cerebral tumour does not indicate that the tumour is a cholesteatoma, and for this reason the nondescript term "cholesteatomatous tumour" (or cyst) is better avoided.

Dermoids and the hair-containing cholesteatomata.—Throughout the literature the relationship between the cholesteatomata proper and the intracranial dermoids has been often discussed. Although in the majority of instances the epidermoid tumours are made up of epithelial tissue which corresponds with the superficial or epidermal layer, nevertheless there are cases on record in which hair has been seen in tumours otherwise quite typical. Thus Bostroem, Horrax and others have

recorded cases in which typical pearly cholesteatomata have contained hair. In some there may also have been sebaceous glandular structures present in the neoplasm associated with the hair follicle. Horrax, in a recent paper on this subject, states that the depth of the epithelial cell layer which constitutes the tumour anlage, determines the structure of the subsequent neoplasm. Where the developmental layer has been purely epidermal, there will result the ordinary pearly cholesteatoma or epidermoid, as in our present cases. But if a deeper or dermal layer is concerned, then the other structures, which characterize a dermoid type of growth, will occur in the tumour. Amongst the latter are included the hair-containing tumours. Horrax would classify them all as cholesteatomata, and further specify them as hair-containing or non-hair-containing. Three cases are cited by the author, the first two of which are dermoids and are outside the strict scope of this paper. In the third case, however, the tumour was typically pearly in appearance; it lay in a characteristic site and presented the ordinary histological picture, except for the finding of hair, glandular tissue and a little bone.

Bostroem dealt at some length with the relationship between dermoid and epidermoid growths. In the latter type he was insistent that all the tissue elements should be of epithelial nature. He regarded the dermoids—which contain mesoblastic structures—as arising from a dermis which differed not in actual depth of layer, but in embryological antiquity. A younger and more primitive cell layer, he suggested, will give rise to both epithelial and mesothelial tissues, and will be characterized by a dermoid rather than an epidermoid type of growth.

It seems obvious from the standpoints of both embryology and histology that there cannot logically be any strict or sharp line of demarcation between the epidermoids and the dermoids. Both are primarily epithelial tumours resulting from cell-inclusions, and the resulting structure will depend upon one of two factors. In the first place, the depth of the primitive layer may be the critical factor—the epidermoids arising when the epidermal tissue alone is concerned and the dermoids when the deeper dermal layer is in question. The hair-containing epidermoids—e.g., Horrax's third case—may represent a transition form. On the other hand the age of the primitive layer may be of more importance than the actual depth. Thus, for example, a dermoid type of tumour may result when the cell inclusion takes place at an early embryonic date, while cell inclusions occurring later in foetal life tend to subsequent epidermoid growths.

If, however, there is but little histological or embryonic distinction between the dermoids and the epidermoids, there appear to be certain points of differentiation from both clinical and anatomical angles. Thus the age factor is of importance, dermoid tumours causing symptoms at an earlier date than the epidermoids. Secondly, the site of origin is important; the epidermoids tend to originate at or near the midline, from the base of the brain, and frequently in association with the third or fourth ventricles. Dermoid tumours, on the other hand, are not uncommonly situated within the substance of the cerebral hemispheres, and may be multiple. The dermoids more often break down in the centre to form cysts, and they are less often covered by the characteristic nacreous sheen. Lastly, the dermoid variety of growth is more often associated with other congenital anomalies and developmental errors.

The. cholesteatomatous endotheliomata.—Under the above title Blumer (1900) described two tumours attached to the choroid plexus of a man aged 59. The clinical history is not important. At autopsy, some degree of ventricular distension was seen. Attached to the left side of the choroid plexus was an ovoid nodular mass measuring 2.2×1.5 cm. The cut section was mostly mottled and reddish-grey, but numerous small yellow areas were present. A similar tumour measuring $1.8 \times 1.2 \times 1$ cm. lay in the right lateral ventricle. Numerous gritty particles escaped from the cut surface of the mass, which proved to be cholesterol in composition.

Blumer described two distinct histological parts in the tumours, a cholesterol-free and a cholesterol-containing portion. The former was small and situated peripherally, and constituted the nodules which appeared on the surface. Small round or oval spaces associated with the blood-vessels, and containing one to three cells, formed the characteristic feature. The cells were ovoid with a relatively small nucleus; the protoplasm contained fine refractile granules.

In the cholesterol-containing part of the growth were numerous wedge-shaped empty clefts which presumably held cholesterol in the fresh state. Red blood-cells, a few leucocytes and occasional tumour cells, occupied the intervals between the spaces. Changes in the connective tissue gave rise to multinucleated cells, the shape of which depended upon the accommodation between the clefts. In the older portions of the tumour the cholesterol cavities had become narrowed by contraction of newly-formed connective tissue.

Blumer regards his neoplasm as commencing by a proliferation of the endothelial cells of the perivascular lymph spaces, followed by a

gradual thinning of the walls with subsequent escape of blood into them. Cholesterin crystals then appear in the blood-infiltrated tissue; finally, a proliferative process takes place in the connective tissue.

It is obvious from the minute description that this tumour differs markedly from the epidermal tumours forming the subject of this present paper. As Blumer points out, there is an obvious resemblance to the equine psammomatous tumours, and the two growths are probably identical. The author arrives at the important conclusion that there probably does exist a class of cholesterin-containing tumours of the choroid plexus in the human which he proposes to call cholesteatomatous endotheliomata.

Does Blumer's case constitute the solitary example on record of such a tumour? Or is it possible that the cholesteatomatous neoplasms seen by Klebs, Perls, Nehr Korn, Frank [15] and Schmaus and others, who have supported an endothelial origin, were actually tumours of the Blumer variety?

The middle-ear cholesteatomata (cholesteatosis).—By far the largest class of new growths spoken of as cholesteatomata is found in association with diseases of the middle ear; otologists have for many years been familiar with the occurrence of tumour-like masses of epithelial debris, occurring either in the cavity of the middle ear or in its immediate vicinity. There is less certainty as to the exact mode of origin of these formations, and as to the relative importance of various ætiological processes in their causation.

A chronic inflammatory otitis media is almost always associated, and a perforation of the tympanum is practically constant. The aperture is usually present in the postero-superior quadrant of the drum, or else in the membrana flaccida of Shrapnell; cholesteatomata are rarely associated with perforations through the lower half of the tympanum.

There are two main types of cholesteatoma described in this connection; first, there may be an irregular, caseous mass without any definite capsule, composed of epithelial cells, "squames," fat, blood-cells, granulation tissue, bacteria and cholesterin-crystals. Secondly, the tumour may be compact and lamellated, and possess a definite capsule with a brilliant mother-of-pearl sheen. It is probable that this second variety is merely a later stage of the first. The cholesteatomata frequently become infected, and break down in the centre to form a pultaceous and foul-smelling debris.

Both varieties of neoplasm are usually encountered within the antro-tympanic cavity. As the tumour increases in size, it compresses and

finally erodes the surrounding bone and may thus invade the mastoid antrum; sometimes the posterior wall of the cavity is destroyed and the tumour invades the cranial cavity. Here it may grow apace and extending backwards push aside the dura and sigmoid sinus, and distort the occipital and even the cerebellar lobes.

Many speculations have arisen to explain the origin of the aural cholesteatomata. Von Tröltsch (1868) regarded them as retention tumours; Wendt (1873) thought them to be products of desquamatory inflammation of the mucous membrane of the middle ear. The main difficulty has been to explain how a tumour composed of stratified and horny epithelial cell elements could arise in a cavity lined by columnar epithelium. Two main views are held to explain this phenomenon:—

(1) Habermann (1881), Bezold (1889), and others, believe that the tumours arise from a backward growth of meatal epithelium, through the tympanic perforation into the antro-tympanic cavity, where, possibly under the influence of toxin stimulation, the epithelium takes on the habit of abnormal growth. Other contributory factors probably are inadequate drainage, whereby the products of excessive desquamation cannot be removed sufficiently quickly.

(2) Many objections have been raised against this view. It has been pointed out that mere epidermal invasion of the middle ear is not sufficient to cause cholesteatomatous growth, for Schwartz (1878) had described epidermic blind pouches jutting into the middle ear and persisting throughout life without tumour formation. Again, there are cases—rare it is true—in which no perforation of the drum is demonstrable through which epidermal invasion can take place. Consequently the theory of metaplasia of the antro-tympanic mucous membrane arose; it is supposed that under the influence of some added factor the columnar epithelium lining the middle ear alters in character and takes on abnormal habits of growth. This point of view has been lucidly expounded by Wingrave [62] (1910), who suggested that this metaplasia is brought about by the prolonged admittance of air into the antro-tympanic cavity, which by lowering the aqueous tension causes desiccation of the mucous membranes. In time this drying process, supplemented by the irritation of bacterial and cytolytic toxins, brings about a true transformation of the mucous membrane. Wingrave compares this mechanism with the well-known phenomenon whereby rectal and nasal polyps which, when they protrude permanently from the orifices, undergo a transformation of their surface columnar epithelium

into a stratified or horny type. The same additional factor of inadequate removal of desquamation products of course plays an important part.

Kutvirt's [27] views as to the origin of the cholesteatomata of the ear are interesting. He attributes the primary change to the necrosis of the bone with cavity formation; the mucous membrane lining the original cavity becomes transformed into stratified epithelium. Accumulation of the desquamated scales leads to the formation of the cholesteatoma.

In recent years, however, Nager, of Zurich, has swung the pendulum of otological opinion back to the view of meatal epidermal ingrowth, for by a beautiful histological preparation he was able to demonstrate beyond any doubt this migration of epithelium through a perforation into the cavity of the middle ear.

A third and very rare type of cholesteatoma is known to the otologists; this variety, originating within the air cells of the mastoid, seems to grow without the additional factors of sepsis and tympanic perforation being required. Thus Lucae (1886) recorded a cholesteatoma arising in the mucous membrane of the tympanic cavity: there was no perforation of the drum and the patient had never suffered from ear disease. Two similar cases were reported by Erdheim. Kuhn reported the case of a man aged 51, who for a year had suffered from tinnitus, deafness and vertigo; the patient then developed a cold which led to a suppurative otitis media and later to a mastoid abscess. Exploration of the mastoid cells revealed a cholesteatomatous tumour, the size of a hen's egg, pressing against the cerebellum and sigmoid sinus. Korner removed a cholesteatoma twice as big as a hen's egg from the interior of the petrous bone. Other cases of so-called "congenital" cholesteatoma (or "cholesteatomum verum") have been recorded by Mondscheim (1911), Hennebert (1912), Maasse (1912), Arbantschitsch (1912), Moller (1918), Shefferd [52] (1922), and Karlefors [24], (1925).

Kirchner (1881) demonstrated by sectioning the bony walls surrounding the ordinary type of middle-ear cholesteatoma that the tumour mass insinuates itself through the interstices of the Haversian canals. It is conceivable that those cholesteatomata which appear to arise primarily within the pneumatic cavities are in reality extensions of the stratified epithelial ingrowth from the middle ear. The more usual view, however, is to regard these air-cell cholesteatomata as primary tumours originating from cell-rests. Presumably then, epithelial rudiments are present in the mucous membrane lining these cavities.

At a later stage we shall discuss the occurrence of cholesteatomata within the diploë of the skull bones at a point far removed from the ear. In such cases there seems to be no question of an origin from intra-osseous cavities lined by mucous membrane. The possibility of the petrous and mastoid cholesteatomata being examples of the larger class of diploic cholesteatomata, although rarely discussed by otologists, requires investigation.

The histological structure of the aural cholesteatomata (both "primary" and inflammatory) bears a close resemblance to the meningeal varieties. The nacreous outer layer is made up of a thickened fibro-vascular stratum in which a few plasma-cells may be visible. Lining this is a layer of stratified epithelium resembling the Malpighian layer of the epidermis. The cells are successively columnar, spheroidal and polygonal from below upwards. Eleidin granules, prickle-cells and papilla formation still further enhance the resemblance to the skin. The bulk of the tumour—corresponding with the horny layer of the epidermis—is made up of closely packed and laminated "squames"; the nuclei are either absent or else only faintly visible. Between the cells lie granules of fat and cholesteatomatous crystals (Wingrave).

Although the clear description given by Wingrave recalls in almost every particular the histology of the pial epidermoids, Bailey believes that the two types of growth can be distinguished and—in spite of the descriptions given—states that there is no epithelial sac and no innermost area of plant-like cells in the aural cholesteatomata. Humiston, too, states that the true neoplastic formation is distinguishable by the presence of a newly formed cyst cavity and wall. We were unable to demonstrate any epithelial cell-layer in the sections of an aural cholesteatoma kindly given us by Mr. Hugh Cairns; the specimens consisted mainly of concentric laminæ which closely resembled the area cornea of the epidermoid tumours.

In view of the important rôle played by chronic sepsis in the formation of the aural cholesteatomata, some distinctive term seems necessary. The nature of the tumour is comparable with the granulomata, in lying midway between the purely inflammatory swellings and the true neoplasia. Humiston and Piette [21] described the middle-ear tumours under the appellation "cholesteatosis," a term which we consider both distinctive and adequate.

Cholesteatoma vasculosa in the horse.—Veterinary medicine has long been familiar with the occurrence of intracranial tumours, which are largely composed of cholesterin and have been termed

cholesteatomata. Gamgee (1859) was perhaps the first to describe such neoplasms, and since that date many other cases have been recorded. According to Dextis, indeed, such tumours were found in 22·5 per cent. of 204 cases examined.

The horse is the animal usually afflicted. The tumour is almost always bilateral and appears to arise from the choroid plexus, to which it is attached by a very fine pedicle. Most of the growth floats loosely in the lateral ventricles, being merely tethered to the choroid plexus. In many instances there are no clinical symptoms, though in some cases the horse has been regarded during life as somewhat stupid and confused; in other cases "staggers" have been noted; rarely does any actual paralysis result.

McCarthy [31] (1904) stated that cholesterin depositions were comparatively frequent in the choroid plexus of animals although rare in man, and he suggested that this deposition process was analogous to calcification in the human subject. Corpora amylacea—common in the choroid plexus of man—are rare in animals.

It is obvious that the histological structure of the equine cholesteatoma is entirely different from the ordinary pial epidermoid in man. The tumour is excessively vascular, contains melanin pigment and is made up of endothelial cells.

Schmey has associated the horse tumours with the xanthomata, and regards them as "Granulationsgeschwülste." Joest confirms this view, and explains the formation in this way: first, the choroid plexus becomes infiltrated with macrophages; crystalline deposits of cholesterin then follow, and set up a connective tissue reaction in their immediate vicinity.

Although the term cholesteatoma has been extensively used in the past by veterinarians, and is in fact still in common use in France, M'Fadyean [32], in 1902, pointed out that this term was misleading. He emphasized the dissimilarity in character between these ventricular tumours and the human cholesteatomata, and proposed that the former should be termed psammomata, although he suggested that they were not identical in structure with the human neoplasms of that name.

The histological structure of an equine cholesteatoma, which was kindly given to us by Professor Hare of the Royal Veterinary College, is illustrated in fig. 5. The bulk of the neoplasm was made up of new-formed connective tissue containing numerous cholesterin clefts. Blood-vessels were abundant throughout the section. In no part of the specimen at our disposal could we find any trace of endothelial cell elements or of epithelial tissue.

Are we justified in assuming that these horse tumours all belong to this psammoma group? M'Fadyean's work in this connection suggests that we are not. In 1902 he reported a case of intracranial growth occurring in the horse and approximating in histological structure to the true meningeal cholesteatoma of man. A second similar case was recorded by himself in 1911 [33]. In his first paper he described the brain of a horse which during life showed some evidences of stupidity. Lying within the posterior part of the left cerebral hemisphere was a cyst the size of a pullet's egg. A thin but tough fibrous envelope surrounded the cyst, which was lined by peculiar glistening superimposed

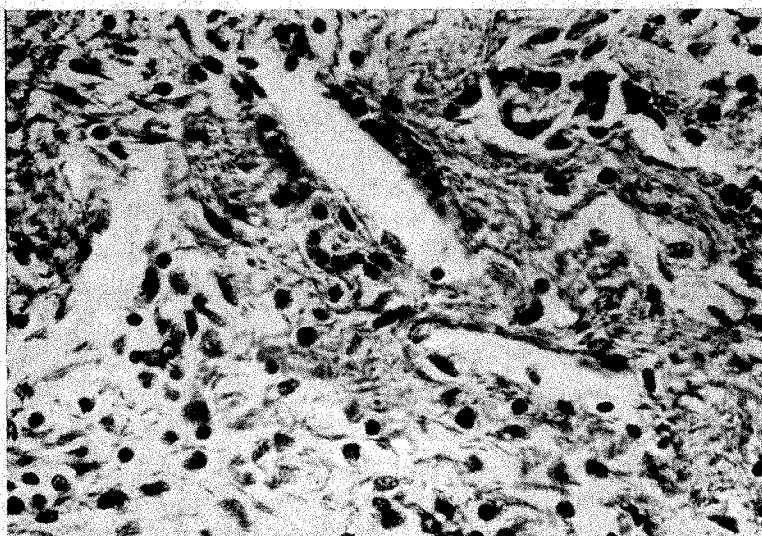


FIG. 5.—Section of a so-called "cholesteatoma of the lateral ventricle" from a horse. Empty cholesterol clefts are surrounded by a cellular connective tissue. No epithelial elements occur.

laminae—resembling fish-scales. This lining membrane proved to contain no cholesterol. Histological examination revealed an external vascular connective tissue layer bearing many pigment-laden cells within its meshes. The inner layer was epithelial in nature, being composed of several strata; the deepest strata contained cubical or short columnar cells recalling the deepest cell stratum in the skin or mucous membranes. Transitional cells occupied the next two or three layers and led to the layer of cornified cells converted into thin scales without any trace of nuclei, corresponding with the stratum corneum of the skin. It was obvious that the laminated horny mass lying free within the cyst cavity was the product of exfoliation of this horny layer.

M'Fadyean's second case was of a mare which showed some unusual behaviour at the age of 11 years. It improved after two months, but then relapsed into a state of dullness which persisted up to death, one year later. At the autopsy a cystic tumour was found lying in the right cerebello-pontine angle. Blood had extravasated between the tumour and the cerebral hemisphere, and there had been some hæmorrhage into the growth itself. The contents were brown, putty-like and somewhat greasy to the touch. Microscopical examination of the cyst wall revealed a connective tissue membrane surrounding a typical epithelial layer. No hair follicles or glands were present. His paper is illustrated with very good photomicrographs, which confirm the similarity in structure between this case and the human epidermoids. Through the kindness of Professor Hare we were enabled to examine the actual specimen at the Royal Veterinary College.

M'Fadyean's two cases constitute, as far as we have been able to trace, the only instances of true epidermoid tumours in the horse. It is possible that the tumours were of dermoid character, particularly the first case, which we are told grew within the substance of the cerebrum, but the histological description contained no mention of any mesoblastic elements.

The diploic cholesteatomata.—Tumours of cholesteatomatous nature growing within the diploë of the skull bones constitute a small and uncommon group. One of the original cases recorded by Müller [1838] was of a cholesteatoma originating between the tables of the temporal bone. At least ten other cases of this nature have since been described.

The neoplasm apparently originates in the diploë, and in its growth expands both the outer and inner tables. A characteristic pearly appearance is obvious when the thinned, overlying bone is removed. Histological reports, though lacking in detail, apparently indicate that the characteristic epidermal elements are present and that the tumours are of typical cholesteatomatous nature.

There are many clinical points which characterize these diploic tumours. In the first place, trauma seems to play an important active rôle. In at least four of the cases (see table) there was a history of a blow on the head of some severity. Shortly afterwards a swelling appeared below the site of the trauma and increased in size. The lump was tender and at times soft in the centre, with a sharp-edged circumference. Skiagraphy revealed a characteristic change in the cranium. Little or no disability may result from this tumour, at least until many

years have passed; and even when the patient seeks advice the signs of focal disease and generalized increased pressure are only slight. Lastly, a feature of the diploic cholesteatomata lies in their amenability to surgical procedures. In at least eight of the cases the tumour has been removed in toto, without a fatality—a result which contrasts strongly with the usual variety of cholesteatoma. Esmarch's case—the first cholesteatoma to be treated surgically—was of a diploic tumour. We have met with no instance of a diploic tumour in our series.

Reference has already been made, when dealing with the aural cholesteatomata, to the occurrence of primary tumours within the pneumatic cavities without the apparent intervention of sepsis as an aetiological factor. It was suggested that these primary neoplasms may be examples of the diploic cholesteatomata originating in the bones around the ear. If this view is correct, then, to the cases recorded by Müller, Virchow, and Pfannenmüller (in which the cholesteatomata lay in the diploë of the temporal bones) must be added those described by many otologists, particularly Lucae, Erdheim, Kuhn, and Shefferd.

THE DIPLOIC CHOLESTEATOMATA.

Author	Reference	Sex and age	Localization	Duration	Symptoms	History of trauma
Müller	Ueber die feineren Bau, &c., 1838		Temporal	—	—	—
Esmarch ..	A. f. p. A. 1856.20.307	M. 24	L. frontal	14 yrs.	—	—
Weinlechner	W. k. W. 1889.7.136	M. 45	Frontal	37 yrs.	Epilepsy swelling	Blow on head at age of 8
Wotrubá ..	W. k. W. 1889.7.889	M. 22	R. frontal	—	Deformity of R. eye	—
Pfannenmüller. .	1893	—	Temporal	—	—	—
Koener	Z. f. Ohr. 1900.37.352	M. 41	L. occipital	Many years	Headache Swelling	—
Blecher ..	D. Z. f. Ch. 1903.70.352	M. 24	L. parietal	10 yrs. +	Headache Swelling	Blow on head as a child
Borchardt ..	A. f. kl. Ch. 1905.77.892	—	—	—	Headache + cerebellar signs	Scalp wound
Cushing ..	S. G. O. 1923.34.557	M. 40	L. temporo-parietal	4 yrs. +	Headache sl. R. hemiparesis	(1) G.S.W. head 10 yrs. (2) Concussion 4 yrs.

NOMENCLATURE.

Not the least of the problems arising during a study of this class of tumour has been the question of nomenclature. At present there is a tendency for the terms "cholesteatoma," "pearly tumour," and even "endothelioma" and "psammoma," to be used synonymously; and furthermore there is a general lack of precision as to the exact meaning of each expression.

The first title, namely, "tumeur adipociriforme," we owe to Le Prestre, but it never gained acceptance.

One of the most generally used terms is that of "pearly tumour." As we have seen, Cruveilhier was the first to use this expression, and in his original paper he laid some emphasis upon the external appearance of these growths. Virchow, writing some five and twenty years later, followed Cruveilhier and spoke of these tumours as "Perlgeschwülste." This title, however, did not gain much popularity at that time, although Rindfleisch, in 1886, employed the modified expression "Perlkrebs." Nehr Korn was almost the only German writer to follow Virchow in speaking of these tumours as Perlgeschwülste. In recent times, Percival Bailey has revived Cruveilhier's original title, and everywhere refers to the "pearly tumours." Bailey gives several good reasons for this: "pearly tumour," he argues, describes accurately the most obvious external characteristic; it describes a feature which is constant; and, lastly, it is non-committal and does not involve any theoretical and unproved consideration of histogenesis, or of site of origin.

Certain arguments may be raised against this nomenclature, however; in the first place, the term "pearly tumour" is purely descriptive, and refers merely to the presence of a glistening nacreous capsule, which in an occasional case may be poorly developed or inconspicuous; secondly, in museum specimens the sheen tends to wear off after immersion in formalin, and in cross-section specimens the pearly capsule may be difficult to find. But more tangible argument is justified when we consider that other discrete though allied growths may have an identical capsule; thus the dermoid tumours, the encapsulated aural cholesteatomata and some of the cholesteatomatous endotheliomata may have similar external appearance, and yet these tumours are separate both in histology and in origin. Finally, Bailey's last argument is a double-edged one; a term which is avowedly non-committal is for that very reason unscientific and undesirable. No hint is given by the term as to

the histological structure of the tumour—a question which to-day seems capable of solution.

The second widely accepted term is *cholesteatoma*. This is probably the most popular title in modern use. Objections against its employment are clearly manifold, and in fact there is but little to recommend it. All writers agree that *cholesterin* plays no essential rôle in the histology of these growths, while *cholesterin* may be present in abundance in many other varieties of intracranial tumour. Secondly, we have seen that there are at least seven different types of growths which are still spoken of as "*cholesteatomata*." And lastly, this appellation is again a purely descriptive one and gives no inkling as to their histology or origin. Horrax, it is true, has partly amended this defect by prefixing the adjective "*meningeal*," but the result still falls short of the ideal.

Bostroem made the most serious attempt at a scientific nomenclature with the expression "*pial epidermoid*." This title did not receive the recognition it deserved however, and to-day it is but little employed. Bailey's chief objection was to the implication it carries: that these tumours are epithelial in structure, and secondly that they arise from the pia. Both assumptions are, according to Bailey, not yet beyond question.

Of the epithelial origin of the usual type of *cholesteatomata*, of which the nine present cases are examples, we think there is but little doubt. For this reason there can be no objection against the word *epidermoid*. A *pial* origin, however, we agree, is not only doubtful but even improbable. We would suggest therefore that these tumours be spoken of as "*epidermoids*" quite simply: such a term is terse, accurate, and conveys the idea of their epithelial nature. The word can be used in ready contrast with the *dermoids*, which are tumours of analogous origin, but contain elements other than mere epidermal structure.

Confusion need not necessarily arise between the *epidermoids* and those epithelial tumours arising in association with the foetal cranio-pharyngeal duct. We already know sufficient of the latter class to be able to separate off a distinct subtype—the *adamantinomata*—which probably constitutes the majority. For the remaining types, we may meanwhile employ some non-committal term such as "*infundibular tumours*," or "*epithelial growths of Rathke's pouch*," until a scientific and accurate classification is forthcoming.

THE CLINICAL ASPECT OF EPIDERMIDS.

In Tooth's series of 258 cerebral tumours, there was one cholesteatoma, and in Bernhardt's series of 487 cases there was only one. Out of 550 tumours recorded by Bailey, and 750 recorded by Horrax, there were two cholesteatomata in the former series and seven in the latter. Schulgin [51] (quoted by Meyer) gave the incidence of epidermids as 0.04 per cent. of all cerebral tumours.

Less than 100 cases of intracranial cholesteatomata have been recorded in the literature; we consider, therefore, that this type of tumour is sufficiently rare to warrant the publication of eight other cases. In addition, a cholesteatoma occurring in the spinal canal is reported later in this communication.

Two or more tumours of this nature have been found on a few occasions, either in the brain or in the spinal cord; in other cases, again, tumours were found both in the brain and in the spinal cord. Carl Frank [14], in 1890, quoted cases recorded by Ladame, Eberth and Eppinger. In Ladame's case there were three tumours—two in one lateral ventricle, attached to the corpus callosum, and one nearby. Several tumours—the size of seeds—were found by Eberth in the region of both Sylvian lobes. Reference will be made, in the section on Spinal Cholesteatomata, to the multiple brain and spinal cord tumours, recorded by Eppinger, Trachtenburg [56], and Raymond, L'Alquier and Courtellemont [46].

Below we give, in detail, the histories, clinical findings and results of eight intracranial cholesteatomata.

Case 1.—Epidermoid of the left ponto-cerebellar angle.

H. G. M., male, aged 27, was admitted to the National Hospital, under the care of Dr. Risien Russell on October 29, 1920. He was well until May, 1920, when he noticed an unsteadiness in his gait. About three weeks prior to admission he suddenly became deaf in the left ear; a week later headache and vomiting commenced. He also complained of a vague difficulty in swallowing and of a mistiness of vision of three months' duration.

The family history was good and, apart from trench fever, he had no previous illnesses. While in the Army in 1916, he was frequently being corrected for holding his head to the left.

On examination he proved himself to be an intelligent man, whose cerebration and co-operation were excellent. He had papilloedema of both discs, with nystagmus, coarse to the left and fine to the right. There was slight dulling to pin-prick over the left side of the face and the left masseter muscle did not contract so well as the right. A watch could be heard at 4 ft. on the right

side but only 1 in. on the left. Further investigation demonstrated that the deafness was due to a lesion of the auditory nerve.

No abnormality was detected in the motor and sensory systems of the arms, legs or trunk. All the tendon reflexes were brisk and equal; the abdominal reflexes were absent and the plantar responses were extensor. The Wassermann reaction in the blood was negative.

A diagnosis of tumour of the left ponto-cerebellar angle was made and Sir Percy Sargent operated on January 28, 1921. A pearly tumour was seen in the left lateral recess, lying beyond the eighth nerve and with the thinned and flattened fifth nerve spread over it; a portion of the tumour was removed. The operation note says that everything was satisfactory. Unfortunately, the patient died later the same day as a result of primary hæmorrhage.

On post-mortem examination the pearly tumour, of which the postero-superior portion had been removed, appeared to be growing inwards into the internal auditory meatus. It covered the left and ventral aspects of the pons and its right border protruded from under the basilar artery. The appearance and site of the tumour are well shown in figs. 6 and 7. The histological appearance was that of a true epidermoid.

Case 2.—Epidermoid of the right ponto-cerebellar angle.

T. O'M., male, aged 28, was admitted to the National Hospital, under the care of Dr. Gordon Holmes, on November 9, 1922. He had enjoyed very good health until 1915 when he was "blown up and buried" by a shell. While at the base hospital he suffered with severe headaches, which were followed a few months later by vomiting. These two symptoms have continued on and off since that date, but they have been much worse since February, 1922. In 1919 he began to stagger to the right; one year later he noted deafness in the right ear. In 1917 he had received treatment for paralysis of the right side of the face.

He was a well-nourished man, with a tired, drowsy manner and slow, unmodulated speech. He had complete anosmia on the right side. The visual acuity in the right eye was $\frac{1}{12}$ and in the left $\frac{2}{3}$; the fields were constricted peripherally, and there were six dioptries swelling of both discs. Nystagmus was present, with slow, coarse jerking to the right and a fine rapid movement to the left. He had a definite weakness of the muscles supplied by the right fifth nerve, together with a sluggish right corneal reflex and hypalgesia of the right side of the face. There was weakness of the right facial musculature and complete deafness in the right ear.

The right arm and leg were weak, hypotonic and inco-ordinate in their movements. His gait was ataxic with a tendency to fall to the right. The diagnosis of a right cerebello-pontine tumour was made. On November 17, 1922, Sir Percy Sargent exposed a tumour of glistening "mother-of-pearl" appearance in the neighbourhood of the posterior aspect of the petrous portion of the temporal bone. The greater part of the tumour was removed with a spoon and suction apparatus.

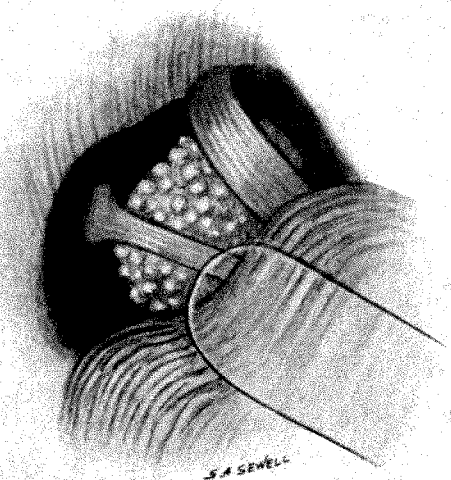


FIG. 6.—Diagrammatic representation of the operative exposure of the tumour in *Case 1*. The flattened fifth and eighth cranial nerves are stretched tightly over the neoplasm. (Drawn from a sketch made by Sir Percy Sargent.)

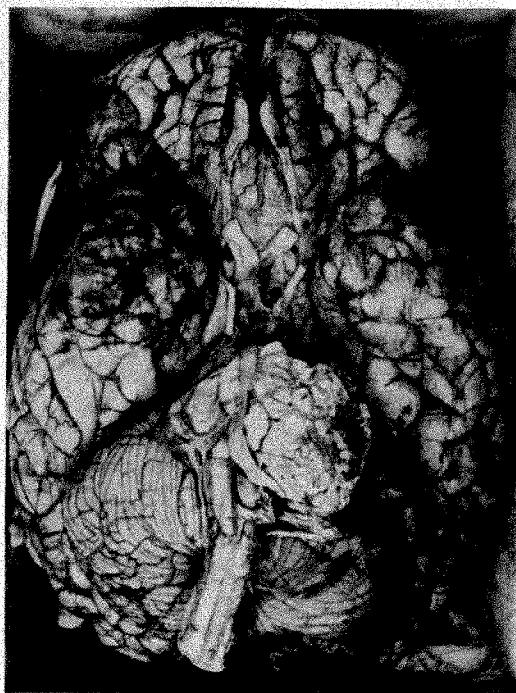


FIG. 7.—Base of brain of *Case 1*, showing a large epidermoid tumour mass occupying the left lateral recess.

The patient died nine hours later from hæmorrhage. On post-mortem examination a typical pearly tumour—the size of a large walnut—lay in the right lateral recess. There was marked indentation and distortion of the right cerebellar hemisphere, and of the right side of the pons and medulla. The fifth, seventh and eighth nerves were stretched and flattened by the tumour, which extended as far forwards as the bifurcation of the basilar artery. Some degree of internal hydrocephalus was present.

The typical appearances of a true epidermoid were seen on microscopical examination.

Case 3.—Mid-cerebellar epidermoid.

C. A., male, aged 37, was admitted to the National Hospital on January 8, 1926, under the care of Dr. Riddoch. He complained of headache, defective vision and unsteadiness of gait of two years' duration. In January, 1924, he began to suffer from attacks of pain in the right occipital region. At the same time the gait became unsteady and the vision in the right eye was misty. After six months' treatment in hospital, he was able to resume his work and remained well until July, 1925, when the headaches and unsteadiness again appeared.

There was nothing of importance in the family history, and he had no previous illnesses.

On examination, he was a well-nourished man of normal intelligence. The visual acuity was $\frac{3}{60}$ in the right eye and $\frac{6}{12}$ in the left. Both discs showed papillœdema and in addition the right disc was covered by a "veil" of connective tissue. The right field of vision was constricted peripherally and contained a large, central scotoma; the left field was normal. Nystagmus was present, coarse on looking to the right, finer and more rapid to the left.

The arms and legs were slightly ataxic, otherwise there was no abnormality of the limbs. The Wassermann reaction in the blood was negative. On February 12, 1926, Sir Percy Sargent removed a large portion of the occipital bone and the arch of the atlas. On opening the dura mater, a glistening mass, which filled the cisterna magna, was seen beneath the arachnoid. The membranes were dissected off and a typical nodular, glistening "pearly tumour" was exposed. A portion of the tumour was removed, but it was impossible to remove the part which was herniated through the foramen magnum.

The temperature rose to 102° on the third day after operation and remained elevated, ranging from 100° to 105° F. until death. He complained of severe headache, backache and neck stiffness; his condition gradually deteriorated, until death occurred on April 15, sixty-three days after operation. The cerebrospinal fluid was examined on six occasions. On February 21, it was a yellow fluid with a fine coagulum and deposit, which consisted chiefly of polymorphonuclear cells. The total number of cells, apart from the coagulum, was 820 per cubic millimetre. On chemical examination, the total protein was 0.18 per cent., glucose 0.022 per cent., chlorides 0.685 per cent. The cultures were negative.

The post-mortem note says: "On removing the skin flap, a quantity of sero-purulent material escaped from an aperture in the newly-formed membrane. Stained films of this exudate showed numerous organisms. On removing the brain, there was no evidence of meningitis. The cholesteatoma, which appeared to be still growing, was situated in the midline between the cerebellar hemispheres."

A sagittal section of the brain is shown in fig. 8. Histologically, this tumour was a true epidermoid.



FIG. 8.—Sagittal section of brain of *Case 3*. The tumour occupies the region of the fourth ventricle.

Case 4.—Epidermoid, posterior end of corpus callosum.

J. S., male, aged 28, was admitted to the National Hospital, on May 20, 1927, under the care of Dr. Grainger Stewart. He complained of headache, dizziness and double vision of three months' duration, although he had not been well since he was taken prisoner of war in 1918. He had appendicitis in 1918, an operation for fistula-in-ano in 1920, and six minor operations on his jaw in 1925.

On examination, he was a well-nourished man of normal mentality. The visual acuity was $\frac{6}{6}$ in each eye, but the visual fields were constricted peripherally, and both fundi showed hæmorrhages and swelling of the discs. The pupils reacted very sluggishly to light, but well on accommodation. There was a bilateral external rectus paresis with well-marked proptosis, but the vertical movements were full.

The muscular and sensory systems were normal, and there was no constant

localizing feature in spite of repeated examination of the reflexes. The Wassermann reaction was negative in the blood and the cerebro-spinal fluid was normal. Examination of the blood and renal efficiency revealed no abnormality.

The diagnosis was doubtful, but in view of the diminution in the visual acuity Mr. Armour made a right fronto-parietal decompression on July 31, 1927. The skull was abnormally thin and the dura mater was very tense. The convolutions over the right frontal lobe were broad and flattened but no tumour was seen or palpated. The patient died later the same day.

On cutting the brain in the sagittal plane, a large round pearly mass was seen extending from above the pineal body to the inferior surface of the splenium of the corpus callosum. It had pushed the posterior wall of the third ventricle forwards and passed as far anteriorly as the foramen of Munro. It



FIG. 9.—Sagittal section of brain of *Case 4*. The tumour distends the third ventricle, which is dislocated upwards and actually lies as an invagination into the lateral ventricle.

measured 4 cm. from side to side, and appeared to arise from an invagination of the meninges between the corpus callosum and the pineal body. Fig. 9 shows the appearance of the brain in sagittal section. The microscopical appearance of the stratum granulosum is seen in fig. 3; the sections showed the characteristics of a true epidermoid.

Case 5.—Epidermoid, right extra-cerebellar region.

M. D., male, aged 41, was admitted to the National Hospital on June 6, 1910, under the care of Dr. Batten. He complained of headache, giddiness, attacks of vomiting and fits, of nineteen months' duration. The family and previous histories were good.

On examination, he was a well developed man of normal intelligence; his speech was normal. The visual acuity was $\frac{1}{10}$ in each eye and the visual fields were full. The edges of the discs were blurred and the right disc was swollen

to three dioptries. Rotatory nystagmus was present on conjugate deviation of the eyes to the right. With the exception of slight inco-ordination in the right upper limb, no other abnormality was detected in the central nervous system.

A diagnosis of right cerebellar tumour was made, and a right cerebellar decompression was performed by Sir Victor Horsley on June 28, 1910. The skull was very thin and the dura mater was under great tension. On July 5, the second stage of the operation was undertaken; an encapsuled glistening tumour was seen beneath the right lobe of the cerebellum. The capsule was incised and its contents—white pultaceous matter—were scraped out.

A fortnight later, the wound was discharging purulent material, films of which revealed polymorphonuclear cells with a few pneumococci. In addition, tumour material consisting of cholesterol crystals and large round epithelial cells exuded from the wound. The temperature ranged from normal to 103° F. Six weeks after the operation, the wound looked quite clean and there was only slight discharge, but the temperature remained elevated and glycosuria was present.

The pulse gradually became weaker, the general condition deteriorated and the patient died on September 18, 1910.

No post-mortem examination was made.

Case 6.—Epidermoid at the anterior end of corpus callosum.

A. H., male, aged 20, was admitted to the National Hospital under the care of Dr. Risien Russell, on May 8, 1916, complaining of headache, dimness of vision and drowsiness.

In February, 1916, he had been suddenly taken ill with headache, vomiting and marked rigidity of his neck. A provisional diagnosis of cerebro-spinal meningitis was made and he was admitted to hospital.

The cerebro-spinal fluid, however, was not turbid and no meningococci were found. His condition gradually improved, until, with the exception of a complete right facial paralysis, he appeared to be well again.

On April 28, the headache and vomiting recurred and he complained of severe giddiness.

Condition on admission, May 8, 1916: he was a short, thick-set lad with slow, hesitant speech and a poor memory for recent events. The visual acuity was $\frac{6}{18}$ in the right eye and $\frac{6}{24}$ in the left. There was bilateral papilloedema. The right eye was proptosed, the left external rectus weak and the right lower face was paralysed.

There was weakness of the left arm and astereognosis in the left hand. The tendon reflexes were sluggish, the plantar responses flexor and the abdominal reflexes were present and equal.

The Wassermann reaction in the blood was negative.

Mr. Armour performed decompression operations in the occipital region on August 8 and August 29. A limited post-mortem examination, which was made on August 29, revealed a typical "pearly tumour" in the midline in the

region of the anterior end of the corpus callosum. The histological appearances were those of a true epidermoid.

Case 7.—Epidermoid in the right parietal region.

E. P., male, aged 37, was admitted to the National Hospital under the care of Dr. Gordon Holmes on September 8, 1921, complaining of weakness of the left arm and leg of fifteen months' duration. His previous illnesses included three attacks of rheumatic fever, pneumonia twenty years previously, and an appendicectomy six years ago. The family history was uneventful, except that his father had committed suicide at the age of 50.

History of present illness.—About fifteen years ago he complained of feeling very languid and tired; severe headache appeared and made him dazed and stupid. He found that he made mistakes in his business as a boot salesman. Twelve months ago he found he could not "control" his left leg, and walking became difficult. The leg improved for a month and then relapsed. About this time he collapsed altogether one day; his head was very bad and he became delirious. He remained fourteen days in bed with marked weakness of the left leg and left arm. Following this, he began to have slight attacks without warning, in which things would drop from his hands and he sat limply in a chair with a vacant expression. His memory and general mental condition were very bad at this time, but have improved considerably since. The headaches have become less frequent and severe during the past seven months, but the left arm and leg have grown weaker. Vomiting occurred on one occasion only.

Clinical examination.—Well nourished, pale man, talks slowly and has difficulty in recalling past events. Emotionally, he appears normal. The visual acuity is $\frac{6}{6}$ in the right eye and $\frac{6}{12}$ in the left. The right optic disc appears a little red and the nasal edge is hazy; the left disc is normal. There is a definite defect in the temporal field in the left eye, the left palpebral fissure is wider than the right and the tongue deviates to the right. The left arm is definitely weak, and there is clumsiness in the hand movements of that side. Co-ordination tests are carried out slowly and inaccurately. The left leg is weak in all movements and there is some spasticity on that side.

All forms of sensation are intact except for astereognosis in the left hand. The arm jerks are present and equal; knee and ankle jerks exaggerated on the left side; plantar stimulation gives an extensor response on the left and a flexor response on the right. All the abdominal reflexes are absent.

An X-ray of the skull revealed a somewhat flattened sella turcica, the posterior clinoid processes of which were eroded. The cerebro-spinal fluid contained 62 cells per cubic millimetre, 0.02 per cent. albumin and the Wassermann reaction was negative.

A diagnosis of right-sided parietal tumour was made, and Sir Percy Sargent operated on October 7, 1921. The skull, which was trephined in the region of the angular gyrus, was thin and brittle; the dura mater was under considerable tension. The gyri were nowhere flattened, but felt softer at a point immediately above the angular gyrus. An incision in this region opened a

cyst lying about 1 inch from the surface. A fairly clear but flaky fluid escaped, carrying up with it a large quantity of laminated necrotic material. It could not be ascertained with certainty whether or not the ventricle was opened.

The cyst contents were reported upon as follows: Yellow fluid contaminated with blood; cells—a few lymphocytes; albumin 0.5 per cent., N.A. ++; urea 0.46 per cent. There is an amorphous mass of rounded bodies in the deposit, giving it a whitish appearance.

The patient stood the operation well. Ten days later he became incontinent; the left-sided weakness was obviously greater, he complained of pains all over and a stiffness at the back of the neck. He was very drowsy. Two days afterwards he was completely powerless down the left side. His mental state was retarded and childish. He improved a little, and three weeks from the time of operation he was able to walk with support; the headaches were returning, however, and the hernia cerebri was growing more tense.

The patient died on December 6, 1921, of broncho-pneumonia.

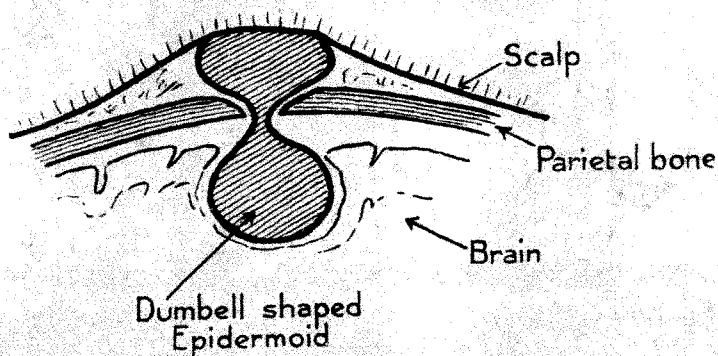


FIG. 10.—Diagrammatic sketch of the tumour in Case 8.

During the first three days following the operation the temperature ranged from 99° to 101°F. It then rose to 103°F. and remained elevated for a fortnight. During the following week the temperature was normal on several occasions, but afterwards he ran an irregular fever until death.

Post-mortem note.—The base of the brain, the area from which the tumour was removed, and the lateral ventricles are full of greenish pus. There is practically a solid abscess lying in that part of the brain where the tumour grew.

The histological appearance of the tumour was that of a typical epidermoid (see fig. 4).

Case 8.—Epidermoid of the right parietal region.

A male, aged 76, was brought in dead to the Casualty Department of the Miller General Hospital, Greenwich, in April, 1928. Apparently he had suddenly collapsed in the street. According to his relatives, who included a

medical man, there had been no previous symptoms whatever, either cerebral or circulatory. At the autopsy, an infarction of the heart wall was discovered, resulting from intense atheroma of the proximal portion of the left coronary artery. When the scalp was stripped from the calvarium, a soft boggy swelling was discovered lying in the region of the right parietal eminence. The mass was in intimate connection with the scalp, for it was torn when the scalp was peeled off, giving rise to an escape of yellow grumous matter. Further examination revealed that the mass lay in a circular depression in the parietal bone, and that the outer table had been extensively eroded. In the centre of this depression was a small circular aperture in the inner table, with a diameter of a quarter of an inch. When the skull was opened a second tumour was found lying immediately beneath the cranial perforation and communicating

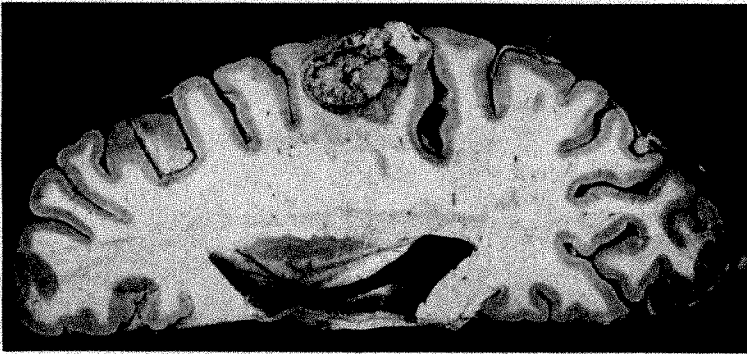


FIG. 11.—Section through semi-ovale of *Case 8*, showing the tumour lying embedded immediately below the parietal cortex.

with the scalp tumour through the foramen in a dumb-bell fashion (see fig. 10). The intracranial tumour lay beneath the pia-arachnoid and in intimate contact with the cortex of the postcentral gyrus. The brain tissue was pushed aside and appeared to be invaded only at the opposite poles of the growth which were buried beneath the surface of the hemisphere. Cross-section of the brain revealed that the tumour was the size of a walnut and contained a pale-yellowish caseous-like material. There was a definite capsule with a typical mother-of-pearl sheen (see fig. 11).

We have examined these cases and the cases recorded in the literature in an endeavour to determine whether there was any feature by which the nature of the tumour could be forecasted prior to operation, or whether, on recognizing the nature of the tumour at operation, the mode of procedure should be modified. Special attention has been paid to the following points: age, sex, previous history, duration of symptoms, presence of any symptoms other than the general and localizing signs of

an intracranial tumour, the site of the tumour, presence of mental symptoms, and the occurrence of meningitis after operation. For convenience we have tabulated these results below:—

EIGHT CASES OF CEREBRAL EPIDERMIDS..

Case	Sex	Age	Previous history	Duration of symptoms	Mental state	Site of tumour	Occurrence of "meningitis" after operation
1. H. G. M. ..	Male	27	Good	6 mths.	Normal	L. ponto-cerebellar	Died day of operation
2. T. O'M. ..	Male	28	Good	7 yrs.	Drowsy	R. ponto-cerebellar	Died day of operation
3. C. A. ..	Male	37	Good	2 yrs.	Normal	Mid cerebellar	Localized "meningitis" for two months
4. J. S. ...	Male	28	Many illnesses	3 mths.	Normal	Midline posterior end corpus callosum	Died day of operation
5. M. D. ..	Male	41	Good	19 mths.	Normal	R. extra-cerebellar	Localized "meningitis" for two months
6. A. H. ..	Male	20	Good	3 mths.	Drowsy	Midline anterior end corpus callosum	Died day of operation
7. E. P. ..	Male	37	Many illnesses	15 mths.	Drowsy	R. parietal	"Meningitis" for two months
8. M. . . .	Male	76	Good	No symptoms	Normal	R. parietal	No operation

We would wish to call attention to the following points:—

Sex.—All our cases occurred in the male sex. The occurrence of these pearly tumours is not, however, confined to males. Nevertheless, there does appear to be a more marked preponderance of this type of tumour in the male, when the sex incidence figures are compared with those found in other intracranial neoplasms.

Age.—Seven out of the eight cases occurred in the second and third decades, the average age being 37.

Previous history.—In five out of the eight cases, the patients were very healthy and not abnormal in any way prior to coming under observation with signs of an intracranial tumour. In one case (No. 1) it is interesting to note that, while in the Army, two and a half years before developing other signs, he was frequently being corrected

for holding his head to the left. A tumour in the left ponto-cerebellar angle was found at operation.

In two of the cases there were histories of many illnesses, but nothing to indicate that there was any intracranial lesion.

Duration of symptoms.—It is stated that the tumours are slowly growing, and that, the onset being very gradual, the symptoms are generally of long duration. The average duration of symptoms in the above eight cases was about twenty months—in four of the cases the duration was six months or less.

Mental state.—The earlier writers stressed the frequent occurrence of mental symptoms in cholesteatomata. In none of our cases was the mental state grossly affected; in three cases there was slowness of cerebration and general mental dulling, but not in excess of what one might expect in a patient with an intracranial tumour. We feel that mental symptoms were probably more pronounced in the earlier recorded cases, because operation was then postponed for a much longer period or not undertaken.

The site of the tumours.—In our eight intracranial cases, four were extra-cerebellar, two were in the right parietal region and two in the midline in relation to the corpus callosum. The problem of the favourite sites of the tumours has been dealt with in an earlier paragraph.

From a careful examination of our own cases and those recorded in the literature, we are unable to find any pre-operative features, symptoms or signs which are peculiar to cholesteatomata.

The occurrence of "meningitis."—The occurrence of localized "meningitis" after operation has been noted frequently in cholesteatomata. In three out of seven of our patients who underwent operation, there was evidence, both clinical and pathological, of a post-operative meningeal irritation. In two of the cases the "meningitis" appeared to be localized to the operation area; there was no evidence of a general meningitis. In the third case, E.P., in which a large cyst, full of flaky fluid and laminated necrotic material, had been found in the right parietal region, and in which it was doubtful whether the ventricle had been invaded or not, greenish pus was found at autopsy in the cyst cavity and in the lateral ventricles. In all three cases the patient survived the operation for approximately two months with similar symptoms—drowsiness and irritability, neck stiffness, pains over the body, and gradual deterioration. Of the other five cases, four unfortunately died within forty-eight hours of operation, and in one case operation was not undertaken.

It is difficult to be certain of the exact nature of the pathological change which occurs locally in some of these "cholesteatomata" after an attempt has been made to remove them. There is no definite evidence, from examination of the cerebro-spinal fluid, that it is an infection. It would appear rather to be an irritation of the meninges set up locally by toxic material contained within these tumours. Furthermore, it is of sufficiently frequent occurrence to call for excessive care in the removal of the tumour, in order to prevent the contamination of the neighbouring structures with the toxic contents.

SPINAL EPIDERMIDS.

We have been fortunate enough to observe a case of an epidermoid of the spinal canal. The occurrence of this type of tumour in this situation is distinctly rare; Percival Bailey, in 1920, in discussing the location of pearly tumours, mentions the fact that Chiari described a case in which the tumour was found in the spinal canal.

Previous cases of dermoid and epidermoid tumours of the spinal canal.—The earliest reference which we have been able to obtain concerning spinal tumours of this nature is to a case recorded by Eppinger in 1875. In this case there were multiple tumours of the cord and brain, apparently growing in relationship with the blood-vessels.

In 1883, Chiari [10] reported an intramedullary cholesteatoma in a man, aged 33, who had been regarded as a case of transverse myelitis for nineteen years. The tumour was 4 cm. in length, and lay at the level of the fourth to sixth dorsal segments, chiefly in the region of the central canal of the spinal cord, but it extended outwards at one point to come into contact with the pia mater. There were no associated malformations of the spinal column.

Ten years later Muscatello [39] described the condition found in a female infant, aged 5 months. There were some "cholesteatomatous perles" in addition to a dermoid, lying extradurally and adherent to the periosteum at the level of the fifth lumbar vertebra. A bifid thoracic spine was present in this case.

In 1898, Trachtenberg recorded the case of a man, aged 55, who had complained for four years of symptoms of a transverse myelitis. At post-mortem, multiple arachnoidal epidermoids and dermoids were found in relation to the arachnoid of the cervical, dorsal and lumbar portions of the cord. In addition, cholesteatomata were found in the left Sylvian fossa, in the left frontal lobe, in both lateral ventricles, in the choroid plexuses of the lateral and third ventricles and in the

corpora quadrigemina. There were no associated malformations of the spinal column.

Microscopically, he stated that they resembled the tumours described by Bostroem; epithelial tissue was found in one tumour, but no hair was present.

Further cases were recorded by Ivanoff [22] in 1903, and Raymond, L'Alquier and Courtellemont in 1904. In the latter case, which occurred in a male aged 34, the spinal lesion was associated with dermoids in the right frontal lobe and in the pituitary region. The patient commenced to suffer with headache and vertigo and loss of memory two years before his death. Later he had a fit and developed a spastic gait. The cerebrospinal fluid was then normal. Three months later headache and vomiting recommenced; the cerebro-spinal fluid then showed on centrifugalization a layer of amorphous matter 2 cm. deep, staining black with osmic acid and bluish with hæmatin. On post-mortem examination a tumour in the right frontal lobe was seen which consisted of a milky mass with strands of hair in it. Histologically, the tumour stained black with osmic acid, and there was an epithelial appearance in its wall. Small nodules were present on the spinal cord, in relation to and connected with the pia mater. The spinal cord and brain lesions were similar, and the case was probably one of multiple dermoid cysts.

In 1906, Berka [6] described a tumour—probably a dermoid—which was found in the medullary cone. It was lying in the substance of the spinal cord, dorsal to the central canal; its capsule was in relation to the pia mater. There were no associated malformations of the spinal column. The patient was a woman, aged 27, who had complained of symptoms of a transverse myelitis for eight years.

A pial dermoid—the tumour was attached to the pia by connective tissue—was reported by Harriehausen [18] in 1909. There was a history of symptoms of a transverse myelitis of nine years' duration given by this patient, who was a woman, aged 23. Doubling of the cord was found below the tumour.

Verébely [57], in 1913, related an interesting case in a 15-year-old boy, who had a spina bifida occulta and from whom a congenital tumour in the lumbar region had been removed. The tumour consisted of two cysts, the size of apples, united by a stalk 2 cm. long; the one was connected with the dura mater, the other with the skin. The contents were thick, rich in cholesterin and contained fine hair. The wall of the outer cyst was thick and consisted of connective tissue, lined by

flattened epithelium; the wall of the inner cyst was thinner and lined by epithelium with small papillary excrescences. There was no epithelium in the connecting stalk, which consisted of a loose connective tissue framework with numerous blood-vessels.

Willy Lauterburg's case [28], published in 1922, was an epidermoid in the subdural space and cauda equina, occurring in a boy aged 7. At the age of twenty-two months this child had "acute brain inflammation." The illness had commenced with cramps, vomiting and high fever; this was followed by marked drowsiness, paralysis of the left seventh nerve strabismus, inequality of the pupils, and slight paresis of the left arm. Lumbar puncture showed a turbid fluid containing lymphocytes, and the case was diagnosed as one of tuberculous meningitis. Two months later the child left hospital apparently cured. In September, 1918, when the child was 7 years old, it suddenly became ill again, abnormal coldness and vomiting being prominent symptoms. Later he developed a total flaccid paralysis with Cheyne-Stokes breathing, and died a few days later from heart failure. Lumbar puncture showed seventy cells per cubic centimetre, of which 23 per cent. were polymorphonuclears. At the autopsy, there was a slight internal hydrocephalus, and an old softening in the head of the right caudate nucleus. Foci of encephalitis were found in the pons. A mother-of-pearl tumour, measuring 12 cm. by 10 cm. by 8 cm., of elastic consistency, easily cut and with flattened poles, was found in the subdural space in the region of the cauda equina. With the exception of a minute vascular pedicle, the tumour lay free between the arachnoid and the dura mater. On transverse section the periphery of the tumour was lamellated, and the centre was yellowish; a small portion of it showed an epidermal membrane.

The eleventh case was reported by Marinesco and Draganesco in 1924 [35]. A male, aged 30, was admitted to the hospital in August, 1923, with a history of progressive weakness of the legs, left more than the right, of eight and a half years duration together with some sphincter trouble. In August, 1916, a soft tumour, a cholesteatoma, was found lying under the dura mater; its extent and relations were doubtful. Two months later he could stand. In 1920 he fell and became worse again; in 1921 he was readmitted to hospital. At this time sensibility was lost up to the tenth dorsal segment and there was a band of hyperalgesia, stretching from the sixth to tenth dorsal segments. There were bilateral extensor plantar responses and exaggerated tendon jerks. He died in November, 1923, as a result of septicaemia. At autopsy, tumefaction with a cystic cavity was found at the level of the

tenth and eleventh dorsal segments. The dura mater and leptomeninges were incorporated in the walls of the cyst. The cyst contained a yellow detritus and cholesterin crystals—plaques of cholesterin were attached to the arachnoid. There was degeneration of the posterior columns in the cord above the tumour; below the tumour the cord was normal.

In the present state of our knowledge of the pathology of these epidermoid and allied tumours, and in view of the difficulties which have confronted us with regard to terminology, we have been in doubt as to how many cases of true "epidermoids" of the spinal canal have been recorded. In several of the cases which we have reviewed the pathological data have been insufficient to enable us to state their exact nature (cases of Eppinger and Ivanoff). It is probable that most of them are dermoid tumours. The cases recorded by Raymond, Alquier and Courtellemont, Berka and Harriehausen are almost certainly dermoids and probably also those reported by Muscatello and Verébély.

However, the lesions in the cases described by Chiari, Trachtenburg, Lauterburg and Marinesco and Draganesco are possibly true epidermoids. Bostroem examined a section of the tumour from Chiari's case and pronounced it a typical epidermoid. Trachtenburg said that microscopically his tumour resembled those described by Bostroem, but also states that fat and sweat glands were definitely present.

Case 9.—Epidermoid of the spinal canal.

N. E., male, aged 15, was admitted to the National Hospital under the care of Dr. Gordon Holmes, on July 7, 1927. He complained of weakness and stiffness of both legs of four months' duration. The family history was good.

He was a normal child at birth, but, when 3 years of age, he had an attack of cerebro-spinal meningitis. The onset of this illness was very sudden, with rigors, vomiting and unconsciousness. He was "unconscious" for seventeen weeks, and during that time repeated lumbar punctures were performed and many injections of anti-meningococcal serum were given. However, he made a complete recovery; there were no ocular or aural defects and no mental retardation.

He remained well and strong until the age of 7, when he commenced to limp. He had no acute illness at the time, but the legs became weaker and weaker until two or three months later he was unable to walk or even stand. After twelve months' treatment with massage and electricity, he began to improve, and within eighteen months he was walking almost normally again. From that time until April, 1927 (aged 15), he was perfectly well, save that he limped slightly on his left leg and the left foot was everted.

Mentally, he was considered a normal child, and he progressed well at school. He had no other illnesses.

In April, 1927, he was in bed for three weeks with an attack of influenza, and during that time he complained of a severe ache in his legs. When he was allowed to get up again, he found that he was unable to stand or walk without assistance. There was no disturbance of the sphincters.

On examination, he was a pale-faced, bright, cheerful boy. The cranial nerves and upper limbs were normal. Both legs were spastic and weak; there was a definite sensory level at the eighth dorsal segment. The knee and ankle jerks were grossly exaggerated; the abdominal reflexes were absent and the plantar responses extensor. The patient was able to take two or three steps when supported on both sides. Scoliosis in the lower dorsal region was present, otherwise the spine appeared normal. The report on the cerebrospinal fluid was as follows: Slightly yellow, no coagulum, three cells per cubic millimetre, total protein 1 per cent.; globulin tests were positive, but the Wassermann reaction was negative. An X-ray of the spine demonstrated the presence of scoliosis but no other abnormality.

On July 14, 1927, Sir Percy Sargent performed a laminectomy in the mid-dorsal region. On removing the laminae of the seventh and eighth dorsal vertebrae, the tumour was brought into view. It was yellowish-white in colour, soft in consistency and like very fine sago compressed into a mass. The surface was a dull mat and consisted of innumerable fine scales, which fell off when the surface was flicked. The interior of the tumour was composed of similar scales, but they were moister and glued together. The mass was not enclosed in a capsule, and the greater portion of it was extracted piecemeal. Histologically this was a true epidermoid (see fig. 2).

It was difficult to be certain of the exact relation of the tumour to the meninges, but it was certainly subdural and intimately bound up with the pia-arachnoid. A temperature of 99.2° F. was recorded on the day following the operation; otherwise there was no pyrexia, and the patient made a good recovery.

On discharge from the hospital on December 21 he was able to walk with a little assistance and there was some return of sensation. He wrote to us on May 8, 1928, saying: "The muscles of the legs are now of normal size and the right leg is very strong. I can walk around the house and up and down stairs by myself, in addition, I can walk about one hundred yards with the aid of sticks. The feeling in my legs is the same now as when I left the hospital. My general health and appetite are excellent."

It is interesting to note that there was no evidence that any local meningeal reaction followed the laminectomy, despite the fact that the tumour had to be removed piecemeal.

N. E. gave a history that at the age of 3 he had an illness called "cerebrospinal meningitis," from which he made a complete recovery. At the age of 7, for some unexplained reason, his legs gradually became weaker until he was unable to walk. He again made an almost complete recovery, and remained well for eight years, when the symptoms returned. When we compare this with the histories of the previously

reported cases, we find that the child recorded by Lauterburg had an illness called "tuberculous meningitis" at the age of 22 months, from which he made a complete recovery, and that Marinesco and Draganesco's patient remained fairly well and able to walk for four years after the cholesteatoma was revealed at operation.

The microscopical section showed the tumour to be a true epidermoid with a broad epithelial layer.

SUMMARY.

A study of the cases recorded in the literature makes it obvious that the problem presents many points of confusion and uncertainty. First, the term "cholesteatoma" has been made to apply to several entirely different types of growth; secondly, the nature and sites of origin are disputed points; and, thirdly, there is no uniform nomenclature.

The term "cholesteatoma" has been at various times applied not only to new growths lying in the median excavation of the brain, with a more or less close leptomeningeal attachment, but also to numerous other tumours of such diverse nature as the products of chronic otitic inflammation, ventricular neoplasms in the horse, tumours growing within the skull bone and cholesterol-containing cysts in the region of the infundibulum. Some other tumours, which have by various authors been named cholesteatomata, are certainly dermoids; others are obviously endotheliomata.

The cerebrospinal cholesteatomata, properly speaking, are essentially epithelial growths, which arise not by a metaplasia of arachnoidal cells, but from embryonic cell inclusions. They are allied to the dermoids, but differ in containing tissue elements which are entirely ectodermal. "Cholesteatomatous-endotheliomata" are probably tumours of an entirely different nature.

Various reasons are given for the employment of the term "epidermoid" in lieu of the less definitive and ambiguous expressions, "pearly tumour" or "cholesteatoma."

Details of eight personal cases of intracranial epidermoids are given. In spite of a careful search for any distinguishing clinical features, the results have been negative; the nature of the symptomatology appears to depend solely upon the *site* (as opposed to the *nature*) of the growth.

One personal case of spinal epidermoid is recorded.

In conclusion we beg to thank the physicians and surgeons of the National Hospital, Queen Square, for permission to make use of their cases. Our grateful thanks are also due to Dr. Greenfield, Dr. Weston Hurst and Professor Tom Hare for their kind assistance.

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THE SYMPTOMATOLOGY OF TUMOURS OF THE TEMPORAL LOBE.

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THE difficulty in localizing tumours of the temporal lobe, especially of the right, is generally recognized, but the possibility of resection of a large portion of the right, and even of the left, temporal lobe without noticeable functional disturbance, makes an early localization of a temporal lobe tumour imperative. It is in early stages of tumours of the temporal lobe that even the last resort of neurological diagnosis—ventriculography—gives occasionally no clue as to the localization.

The literature dealing with the diagnosis of temporal lobe tumours has grown considerably since the appearance of Knapp's monograph [11] over twenty years ago. This monograph was the more important since only eight years previously Oppenheim [15] stated: "Wir haben niemals das Recht die Lokaldiagnose Tumor des rechten Schläfenlappens zu stellen." The literature that followed Knapp's contribution has added to our knowledge of the symptomatology of these tumours, but, on the other hand, it has obscured the importance of certain signs pointed out by Knapp. This discrepancy is easily understood when one realizes the intermittent character of many symptoms in the course of an intracranial tumour. It is a fact that many a symptom is present and is of diagnostic significance only during a certain phase of the development of the tumour.

Temporal lobe tumours are not frequent, and it is significant that none of the contributions dealing with the symptomatology of these tumours which has appeared up to date is based on more than a dozen cases; many of these contributions have behind them only single instances. Conclusions drawn from such a limited material are apt to be erroneous, especially if the importance of a certain symptom is emphasized or denied, for no single sign or symptom can always establish localization.

Three stages may be distinguished in the natural history of an intracranial tumour: (1) when there are no signs or symptoms;

(2) when local signs and symptoms are present, and (3) when general signs and symptoms complete the picture. A systematic examination of the symptoms of temporal lobe tumours during their entire course is essential if one is to learn of their value in localization. It is with this idea in mind that I have studied a series of thirty-eight cases of tumours confined to the temporal lobe of patients of the National Hospital, Queen Square, London. The value of this material is enhanced by the fact that all these cases were observed and studied by the same methods, and most of them by the same members of the staff. A correlation of the symptoms and signs presented by these tumours with the anatomical lesions is essential for evaluation of the rôle of the former in the symptom-complex of the neoplasm, and therefore I have selected for this study only cases in which a post-mortem examination permitted study of the gross anatomical features.

Physiologically and pathologically the various phenomena composing the symptom-complex of an intracranial tumour are interdependent, and interwoven to a great degree. However, for purely didactic purposes one may with benefit subdivide them into those resulting from intracranial pressure, from irritation of the neighbouring areas of the brain, and, thirdly, from focal destruction of the involved region. There were seventeen tumours of the right and twenty-one tumours of the left temporal lobe. From a detailed study of the symptomatology of these thirty-eight cases I shall attempt to show the characteristic neurological picture of tumours of the temporo-sphenoidal lobe, the relative value of the various symptoms and signs, and the diagnostic points that serve in the differentiation of a tumour of the right temporal lobe from one in the left lobe. There were twenty-six male patients and twelve female. The average age for the entire series was 47 years; of the male patients 48 years, and of the female 43 years. In the male the ages varied between 29 and 60, and in the female between 29 and 62.

Headache.—Being a symptom of general increased intracranial pressure, headache has received little attention in the study of the symptomatology of temporal lobe tumours. Kennedy states that the nature of headaches is "little more than useless" as regards its localizing value; Niessl v. Mayendorf [14] and B. Sachs [18] have suggested that a definitely localized pain or tenderness on percussion of the temporal region may be a focal symptom. In an analysis of the localizing value of headaches it is important to distinguish between headaches and pain in the head, the first being more or less generalized,

while the latter is a definitely localized sensation referred to the skull and scalp.

Every patient complained of headache, which preceded the admission to hospital by varying lengths of time, ranging from one week to two years, the average being about six months. While the severity of the headaches varied in most cases, they followed a definite course. Early in the disease a sudden jerk of the head or stooping was enough to bring on a sensation of fullness or an actual headache which, however, passed off immediately. Later the headaches appeared in severe bouts, lasting one or several days, and they were followed by complete remissions for days, weeks, or even months. With the advance of the disease headaches became constant, but they were of a more dull character, an occasional throb, mostly in the early morning.

When the headaches were general they appeared first, in order of frequency, in the frontal region, behind the eyes, in the occipital region and occasionally in the vertex. In eight cases the headaches were localized and limited to the side of the tumour. A study of the pathological findings in these cases gave no explanation of this localization. The anatomical basis of headaches in raised intracranial pressure remains obscure; the widely accepted view that the nerves of the dura mater are responsible for it, if it holds true at all, is hardly sufficient to explain the "early morning" exacerbations. It is in the early hours of the morning that the formation of cerebro-spinal fluid is at its highest, and the "early morning" headache may be immediately relieved by a ventricular tap. The not unusual complaint of the patients that the headache "comes from the back of the head, pushes forwards and rests with unusual force against the forehead and behind the eyes," would tend to suggest their origin within the ventricular system, possibly in the choroid plexuses.

Pain or local tenderness of the head was observed in ten cases; with two exceptions this was localized on the side of the lesion. In an exceptional case a right-sided temporal lobe tumour involved the thalamus and produced spontaneous pain on the entire contralateral side of the body. In another, a right-sided tumour caused an enormous left unilateral hydrocephalus with tenderness over the left parietal region and left frontal headache. In the remaining eight cases the pain was limited to the ipsilateral side of the face and head. In two left-sided tumours with erosion of the bony floor of the middle cranial fossa on the left side, the patient complained of painful fullness of the cheek, which was accompanied by definite tenderness slightly above the middle

of the left zygoma. In one case of a left-sided basal tumour which herniated through the widened foramen ovale and pressed directly on the third branch of the fifth nerve, the patient suffered with sharp, shooting pains in the mouth and left side of the face, which were especially severe when the headache increased. In the other four cases a dull pain in the scalp appeared, at first only when the patient was lying on the side of the tumour, but later became persistent. However, in three instances the patients preferred to lie on the side of the tumour while in bed. In all cases local pain preceded the appearance of headaches by months, on an average by about five months.

Vomiting.—Vomiting was a symptom in nineteen patients at one time or another, while in the other half vomiting never occurred. As a rule the appearance of vomiting followed that of headaches after a considerable length of time. Vomiting usually came on in almost daily attacks and then disappeared for weeks or months, or even altogether. The dependence of vomiting upon the severity of the headaches is well established; it usually occurred during the early morning hours when the headaches were at their worst. The intervals between the attacks of vomiting usually coincided with the intervals between the bouts of headaches, but it was not a constant accompaniment of headaches. The so-called "projectile" type of vomiting was rarely observed in this series of cases, and in my experience it is not frequently seen in patients with gradually increasing intracranial pressure. In several instances vomiting was occasionally preceded by disagreeable sensations of smell and taste, which were components of an uncinat seizure.

Papilloedema.—In five instances no changes were seen in the fundi on the admission of the patient to, or during his stay in, the hospital; in all the other cases the discs showed definite oedematous changes. In no case did the swelling measure more than 7 D., the average being about 3.5 D. The controversy of some twenty years ago as to the value in localization of the comparative degrees of swelling of the ipsilateral and contralateral discs is still alive to-day; the findings in this series of cases indicate that the relative amount of swelling of the two papillæ is of no value as a localizing sign. In eight left-sided tumours and seven right-sided the amount of swelling was identical in the two eyes. In seven tumours of the left side the swelling of the left disc was greater than that of the right, and in two cases the swelling was less on the left than on the right side. In six tumours of the right lobe the swelling was greater on the right, and in one instance it was greater in the left. Paton [16] has pointed out the unreliability

of the relative amount of swelling of the discs in lateralizing a tumour, but Horsley [7] attached great importance to it; both supported their contentions with clinical observations.

In the estimating of the relative changes in the fundi one must take into consideration, not alone the papillary swelling but also the hæmorrhages and exudate when these are present. Another source of error lies in too short observation of the changes; from a single examination it is impossible to draw trustworthy conclusions since the degree of swelling of the nerve head may change. In a patient with a right-sided tumour, for instance, ophthalmoscopic examination revealed 2·5 D. swelling in the right eye and 3 D. swelling in the left, but two weeks later the same observer (Dr. Gordon Holmes) found a swelling of 4·5 D. in the right and 3·5 D. in the left; while a second patient with a left-sided tumour showed at the first examination 3 D. of swelling in the right and 3·5 D. in the left eye; next week the same measurements were obtained, but two weeks later the same observer found 3·5 D. of swelling in the right and 2 D. in the left papilla. A careful digest of the records suggests that only a comparison of the incipient signs of papilloedema, that is blurring of the edges of the disc with fullness and tortuosity of the veins, is of importance in the lateralization of the tumour, since they may be found at first in one eye only. When the tumour is far advanced the degree of swelling is usually identical on the two sides, and in the late stages one frequently observes more swelling in the eye contralateral to the site of the tumour. The latter is probably due to retrograde degeneration and atrophic changes in the papilla of the ipsilateral eye where the œdema is of longer standing.

Incontinence.—Tumours of the temporal lobe differ from frontal lobe tumours as regards sphincter disturbances. In a series of thirty frontal lobe tumours controlled by autopsy which I have studied, incontinence was observed in 60 per cent., while in the present series of tumours of the temporal lobe it occurred only in 20 per cent. of the cases. The reaction of the patient towards the incontinence is different in the two series: while in temporal lobe tumours the patient is usually ignorant of the incontinence, a patient with a tumour of the frontal lobe realizes the entire act but cares nothing about it; his judgment of its impropriety is impaired. Incontinence is a much earlier symptom in frontal than in temporal lobe tumours, in which it appears only in the late stages of the illness. While no definite conclusions can be drawn from the influence of the seat of the tumour upon the presence

of incontinence, it is of interest that in all eight cases with incontinence as a definite symptom the tumour was situated at or about the pole of the temporal lobe, extended towards the basal ganglia, and occasionally also pressed upon the frontal lobe. An investigation of these eight cases of temporal tumour indicates that complete incontinence is as a rule preceded by frequent and precipitate micturition; but in one instance incontinence was immediately preceded by retention of urine, which persisted for three weeks.

Psychic disturbances.—Psychic disturbances are of little diagnostic value in intracranial tumours in general, and in tumours of the temporal lobe in particular. They may be the result of prolonged increase of intracranial pressure, or they may accompany destructive lesions of various areas of the brain. In their treatises on the symptomatology of temporal lobe tumours, Knapp [10, 11] and Kennedy [9] analysed the psychic disturbances observed from two opposite angles. While Kennedy subordinates all the psychic disorders to the so-called "dreamy state," Knapp includes them all under the term "Korsakow's symptom-complex."

The usual psychic disturbances observed in temporal lobe tumours are loss of memory and changes in temperament and character; they differ greatly from the "dreamy states." While the latter are temporary, more or less periodical alterations of consciousness coming on in attacks, the true psychic disturbances are more or less progressive, or at least stationary, manifestations accompanying the disease. Dreamy states are epileptic equivalents and will be dealt with under the heading "fits."

From the findings in this series of cases I am inclined to group the psychic disturbances as follows: (a) Defects of memory, (b) change of character and temperament, (c) hypersomnia, and (d) mental confusion. In 19 patients out of the 38 of this series there was definite subjective, or subjective and objective, evidence of deterioration of memory. This is an unexpectedly high incidence, especially when compared with my series of 30 frontal lobe tumours where changes in memory were definite in 13 cases only. In tumours of the temporal lobe loss of memory is a much later symptom than in frontal tumours, for while in the former it appeared on an average two months before admission to the hospital, in frontal tumours the average was six months. No definite relationship could be made out between defects of memory and the precise site of the tumour in the temporal lobe. The nature of the memory defects in temporal lobe tumours is in some respects different

from that in tumours of the frontal lobe. While in the latter the defects concern only recent events, in temporal lobe tumours it is not unusual to find loss for both recent and past happenings. When failure of memory for past events is observed, it is usually accompanied by slow cerebration and inattention; one is tempted to believe that there is not sufficient will power to recall the past.

The opinion has been expressed in the literature that the psychic disturbances in organic disease of the temporal as well as of the frontal lobe are found mainly with lesions of the left side of the brain. Some authors go so far as to say that psychic disturbances associated with tumours of the right frontal or temporal lobe are merely a result of general pressure. An analysis of the findings in the cases I have studied shows that defects of memory were present in 41 per cent. of the tumours of the right temporal lobe and in 57 per cent. of the left-sided cases, while failure of memory was seen in 38 per cent. of the cases with tumours in the right frontal lobe, and in 47 per cent. of those with left-sided lesions. At a first glance these figures would seem to support the above contention, but a similar analysis reveals changes in temperament and character in 24 per cent. of tumours of the right temporal lobe and 19 per cent. of tumours of the left lobe; in 54 per cent. of tumours of the right frontal lobe, and 53 per cent. of cases with a left frontal lobe tumour. This prevalence of defects of memory in tumours of the left side as compared with tumours of the right side of the brain is, I believe, due to the frequency of speech disturbances in disease of the left temporal and frontal lobes. Memories are largely auditory and visual impressions, but when these impressions are not well understood they obviously leave no memories. The more importance one attributes to the localizing value of defects of memory in intracranial tumours the greater is one's disappointment in the end. One gains an impression that memory is much more a function of the brain as a whole rather than of any specific area. That defects of memory occasionally occur in prolonged increase of intracranial pressure, whatever the cause may be, is common knowledge. Probably patients with organic lesions of brain fail to fix or register an impression rather than forget a duly registered one. One can hardly speak of loss of memory in a patient who "forgets" the sensation of a pin-prick immediately after it is felt by him, as was the case in two patients of this series.

Changes in personality were observed in eight patients, or in 21 per cent., as contrasted with 50 per cent. in the series of frontal

lobe tumours. Since the appearance of these changes is usually insidious no reliable facts as regards the time of their development could be secured. However, a perusal of the records gives the impression that these changes appear at a considerably earlier date in frontal tumours than in tumours of the temporal lobe.

The changes in personality observed may be grouped under optimistic and pessimistic tendencies. In the first the patient appears from the beginning as unduly "sociable," loquacious and good spirited, and soon reaches a stage which is known as euphoric. He is cheerful and perfectly happy; he denies or minimizes his present symptoms, and there is often a persistent tendency to facetiousness. In the course of time his jokes become flat, dull and stupid; one patient would constantly seize on somebody's name and add something funny to it, as "Cecil—gristle," while another, when told to sit up, responded, "Sit up, good wife, and shake your feathers." It is interesting that even in a late stage of the disease, when the patient is hardly able to understand a simple command, he may still enjoy stupid catch-phrases of his own fabrication. This is so obvious and strange that it suggests to the observer that the entire mental energy of the patient is given over to this narrow and dull corner of intellectual life.

When changes in personality take a pessimistic shade, the most frequent state is one of depression. The patient is constantly worried over his condition; he becomes self-centred and extremely egoistic; nothing in the world matters if only he could be relieved of his trouble; he becomes irritable and suspicious; he is stubborn, and all suggestions from whatever source they come are met with distrust and suspicion; he suspects the faithfulness of his wife, and loses all interest in his family.

Both trends, the optimistic and pessimistic, finally lead to the condition known as "childishness," or, as the French authors call it, *puérilisme*. Childish interests in toys, plays, and stories, and a rapid transition from one emotional state to the other, as from crying to irresistible laughter and then again to weeping, is the mental state at which the patient arrives in the final stages of the disease.

The literature on prolonged sleep in intracranial tumours, or hypersomnia as Purves Stewart calls it, is very confused, and can be of little assistance in studying this symptom. The term "lethargy," which is used so frequently, is misleading, since lethargy includes not only true prolonged sleep or hypersomnia, but also the stupor which is a common symptom of prolonged severe increase of intracranial pressure. In the

present series hypersomnia was observed in 23 per cent. of all cases. In the tumours of the temporal lobe this symptom appeared on an average one month before admission to the hospital, and in most of these cases there was a history of actually prolonged sleep. In some it was described as extreme drowsiness, apart from headaches, with yawning and persistent nose rubbing. That nose rubbing is to be interpreted as a sign of sleepiness is suggested by observation of infants and small children. The prolonged sleep approximates to that of the symptomatic narcolepsies. It had been for long stated that tumours in the region of the third ventricle are often associated with pathological sleep, but a review of the nine cases of this series allows no definite conclusion on this question. In five cases, however, the lesion was basal and definitely involved the basal ganglia.

Mental confusion was seen in three cases only. One patient, an engineer by profession, persistently refused to believe that he was in a hospital; he was always "on my job." In a woman of 54, in whom mental confusion preceded the admission to the hospital by eight months, the first thing her daughter noticed was that "one morning she served breakfast on dinner plates." The third patient was completely disoriented in time and space, after an attack of severe headache and vomiting about two weeks before death.

Fits.—Although recognized by most authors, fits have not been given as much attention as they would seem to deserve as a symptom of tumours of the temporal lobe. The fact that the various epileptic equivalents which may be associated with these tumours are referred to throughout the literature by different and frequently misleading headings bears witness to it. To be of diagnostic significance a fit must indicate a local discharging lesion; it must have a local beginning, or at least it must allow a conclusion as to the lateralization of the lesion from the state of the reflexes and the condition of the patient immediately following it. It is mainly from this point of view that fits will be discussed below.

Fits of one kind or another were observed in nineteen patients of this series. That epilepsy is not a late symptom in all cases of temporal lobe tumour may be concluded from the fact that the first fit occurred on an average nine months before admission to hospital, the extremes being two weeks in a case of typical local motor seizures and four years in a patient with classical "dreamy states." Among the nineteen cases five had general epileptic seizures, but the onset in one of these cases was gradual enough to allow a lateralization of the discharging lesion, since

turning of the eyes and head to the opposite side always preceded the convulsions. In the other four cases the onset was too rapid and the condition of the reflexes immediately following the attacks too indefinite to allow a conclusion as to the seat of the lesion. Typical Jacksonian fits were observed in two patients; they first occurred late in the course of the disease, as one would expect from anatomical reasons, the average time being three weeks before admission to the hospital. In these two cases the fits commenced in the hand; although they localized the lesion they were of little diagnostic significance because of their late onset. Local sensory fits, including uncinatc seizures, dreamy states, and visual and auditory sensations, are of far greater diagnostic importance.

Focal sensory fits occurred in twelve patients. The average length of time from the first fit to admission to the hospital was over ten months. In some of these twelve patients the fits consisted of combinations of various sensations. Uncinac seizures were seen in seven cases; in three of these they preceded dreamy states, with the more or less complete train of phenomena that accompany them. Dreamy states unpreceded by uncinatc seizures occurred in four cases, and in one instance there was a definite auditory aura followed by a local motor fit. The uncinatc seizures in one case were always ushered in by paræsthesiæ of the left foot; obviously such a combination at once localized the discharging lesion. In the other cases the uncinatc fits, whether followed by dreamy states or not, had a purely localizing but not a lateralizing significance.

In neurology there have been few clinical discoveries that have remained stable and alive as long as Jackson's teaching on uncinatc fits. The dreamy state is a most complex phenomenon which taxes greatly the self-analysing ability of the patient and the observing power and experience of the physician. Only persons with more than average intelligence are capable of observing and expressing in words their experiences during such a state; for the less intelligent it is too elusive, and the most one obtains in a history is a statement from the relatives that sudden attacks occur in which the patient appears "vacant with a lost look and mind." Of course, much depends upon the physician; forty years ago Jackson [8] pointed out that if the physician is waiting for a well-expressed dreamy state he will miss many a typical but slighter seizure. These facts suggest that dreamy states occur much more frequently, but remain unrecognized by the patient and physician.

Under the name of "intellectual aura" the dreamy state was long

known to occur in epilepsy. Jackson was opposed to this term because the dreamy state is not a warning but a striking symptom of a certain variety of epileptic attack. Though much has been written on this complex condition, Jackson's original description is probably the best of all. "This is a very elaborate or 'voluminous' mental state." Along with this mental state there is frequently a crude sensation of smell or taste, or an epigastric or other visceral sensation. Dreamy states are not always accompanied or preceded by uncinatè fits, just as the latter are not constantly followed by dreamy states. There may be in the dreamy state loss of consciousness, or "over-consciousness" co-existing with a defect of consciousness to present surroundings. Such a co-existence of a defect of consciousness (to the present) with an "over-consciousness" (to reminiscences of the past) is not an exclusive feature of this variety of epileptic equivalent, and is in accord with phenomena observed in other epileptic variants. It is a well-established fact that a discharging lesion is accompanied not only by plus function but also by minus function; paralysis or paresis develops at the same time as the clonic movements.

For the description of a typical dreamy state I mention the history given by an intelligent female patient: "At first everything goes black: then I feel as though I am taken miles out of myself. I do not lose consciousness, but everything around me seems to recede into the distance. My family seems miles away; their voices sound as though they are talking miles off. There is a feeling of strangeness about everything, although you are in your own home. These attacks are accompanied by a taste in the throat and a smell in the nostrils like lysol. It is more like fumes coming up my throat." These attacks last about five minutes. They are preceded by "a feeling of warmth in the abdomen and a sensation as though everything inside were turned to boiling water." This sensation in the abdomen is so uncomfortable that she rubs the abdomen; as it passes off it is succeeded by the dreamy state. Immediately after an attack she belches a great deal of gas. Her relatives added that before an attack came on "her eyes looked vacant and bulged."

The dreamy states alone give no information as to the side of the lesion, but the visual hallucinations that may accompany them are of lateralizing importance when they occur in a part only of the visual field, as they are usually observed on the side contralateral to the tumour.

Visual hallucinations in organic lesions of the brain have formed a

most confused chapter in epilepsy. The widely-spread tendency of authors to group together without discrimination all visual sensations has continued for many years and is still occasionally met with in the literature in spite of a warning sounded by Jackson [8] forty years ago: "Before we can make good generalizations we must carefully analyse. To group together as 'visual warnings' colour projections, apparent alteration in the distance of external objects, and 'dreamy states' with definite scenes, is generalizing without previous analysis and is an attempt to organize confusion." For a proper evaluation of the clinical and pathological significance of visual phenomena it is imperative to distinguish crude visual sensations without definite outlines and vivid contents, from complex visual sensations—the true visual hallucinations. The general consensus of opinion to-day is that crude visual phenomena result from discharges spreading over the area striata of the occipital cortex. This discharge is projected to the corresponding point in the visual field and is perceived by the patient in the contralateral half of the binocular field of vision. In these cases the visual phenomenon is the dominating feature in the epileptic fit. On the other hand, complicated subjective visual sensations, the visual hallucinations proper, play only a subordinate rôle in the epileptic fit due to organic brain disease. They are never of the nature of an aura, but appear as one of the train of sensations following upon an uncinate seizure due to a discharging lesion in the region of the uncus. According to Jackson visual hallucinations are provoked by an irritating lesion in the region of the uncus. The interesting question why only an uncinate aura is capable of provoking complicated visual phenomena, while the visual sensations in the course of a visual aura are of a crude and primitive nature, must be left unsolved for the present. Phylogenetically the brain is an appendage of the organ of smell, the rhinencephalon being the oldest portion of the cerebrum; as Gordon Holmes [5] expresses it: "Even in man it (the rhinencephalon) may still serve as a storehouse of simple memories and associations."

Cushing [2] thinks that the visual hallucinations which occur with tumours of the temporal lobe bear some relation to the damage of the optic radiations, since in his cases the hallucinations were always referred to the side opposite that of the tumour, i.e., in the defective halves of the visual fields. In seventy-two cases of temporal lobe tumour from Cushing's clinic, Horrax [6] found visual hallucinations of a "more or less definite and complex nature" in twelve cases, and of a less definite character in five instances. Defects in the visual fields were present in

only five of the twelve cases at the time of the first appearance of the hallucinations. In one case the hallucinations preceded the first appearance of a small quadrantic defect by at least four months; in another case there was no visual defect at any time, and blindness prevented examination of the fields of vision in one patient. In the remaining four patients with visual hallucinations the states of the visual fields are not referred to. While the relationship between visual hallucinations and defects in the visual fields is inconstant, the associations of these hallucinations with uncinæ fits or dreamy states was definitely established in "at least" (Horrax) thirteen cases out of the seventeen. These facts suggest strongly that the association of the hallucinations with defects in the visual fields is merely a coincidence.

What has been said of visual hallucinations also holds true for auditory hallucinations. In the opinion of Holmes [5], subjective auditory hallucinations are rare and less striking than other sensory phenomena. When an auditory aura begins independently of any other sensory phenomena the patient usually describes crude noises, or everything may appear silent. It is only when an auditory sensation follows an uncinæ seizure that complex hallucinations, as of voices, occur. In my series an auditory aura was observed only once; a patient with a left-sided temporal lobe tumour heard on several occasions "horrible noises," which were followed by twitchings of the right foot and leg. The noises were referred to both ears equally. In a recent report [1] from Cushing's clinic, auditory hallucinations were described four times among ninety-nine temporal lobe tumours and six times among ninety-nine frontal lobe tumours. There was no reference in the report to the relations of these hallucinations to epileptic phenomena. The fact that these hallucinations were observed in six patients with frontal tumours, all of whom showed signs of psychosis, suggests strongly that these auditory hallucinations were psychogenic.

Motor and sensory disturbances.—It is obvious that in tumours of the temporal lobe motor and sensory disturbances are neighbourhood symptoms. This fact reduces their diagnostic importance, though they are frequently observed in the course of tumours of this lobe. In five instances of this series a lower facial weakness only was observed. In three other instances an isolated motor weakness of the upper extremity was seen. More extensive motor and sensory disturbances were more frequent. The entire side of the body, including the lower face, arm and leg, were affected in ten cases; in seven instances there was a combined paresis of the face and arm, in three others of the leg and

face, and in two the arm and leg were affected. The motor or sensory disturbances rarely amounted to paralysis or anæsthesia, and in the majority they were so slight as to require repeated examination before they could be regarded as definite symptoms. Their onset was insidious, but in one case a hemiparesis appeared suddenly and was probably due to a hæmorrhage into the tumour. Pure sensory disturbances were observed only in one instance, in which there was complete loss of postural sense on the contralateral side of the body. In two cases tactile hemihypæsthesia was accompanied by facial weakness of the same side. When the sensation of the face was impaired its asymmetry on movement was of no importance, since sensibility is as essential in mimicry as the function of the muscles.

A controversy exists in the literature as to the cause of the motor disturbances in tumours of the temporal lobe, whether the pyramidal tracts are involved in the cerebral peduncles, as Knapp maintains, in the internal capsule or in the motor cortex. The fact that in this series of tumours motor epilepsy occurred in seven cases only speaks for the rarity of involvement of the motor cortex. On the other hand, the frequency of facial weakness preceding the appearance of weakness of the upper extremity, or of both limbs, would suggest the cortical origin of the motor disturbances. The best example of the development of a hemiparesis of this nature was seen in a case with a right-sided tumour in which a left lower facial weakness was followed two months later by a weakness of the left arm, and three months later by weakness of the left lower extremity. While in the cortex the facial centre lies directly over the temporal pole, the topographical relations of the pyramidal fibres in the internal capsule are such that those to the facial nucleus remain far forward and cannot be involved before the fibres to the lower extremity are encroached upon by a tumour advancing from the temporal lobe. It is, therefore, natural to believe that when the motor weakness begins in the face and then extends towards the upper extremity it is a result of a cortical disturbance, but in cases where the weakness appears first in the lower extremity the lesion may be capsular. From anatomical reasons one would expect motor weakness of capsular origin to be combined with a hemianæsthesia and hemianopsia, but this was seen in one case only of the series, in a patient with a deep-seated tumour of the temporal lobe, in whom a slowly developing right hemiparesis was followed by a right hemihypæsthesia and a right homonymous hemianopsia.

Knapp lays much stress upon motor weakness produced by com-

pression of the cerebral peduncle. There were eight instances in this series where the cerebral peduncle or the pons was compressed by the tumour, especially by herniation of the temporal lobe through the incisura tentorii. A careful study of these cases gives little support to Knapp's contention, for in compression of the cerebral peduncle one would expect an involvement of the upper extremity first, but in the three cases with isolated motor weakness of the arm there was no pressure upon the peduncle. Apparently the compression of the peduncle or of the pons is extremely gradual and gives few, if any, physical signs on the neurological examination. In this respect it is of interest to mention three cases where the neurological findings were baffling until the post-mortem examination revealed the true situation. In a patient with a right-sided tumour, a definite weakness of the right side of the face was observed in the later stages of the disease. In another patient with a right-sided tumour the plantar response was definitely extensor on the right and flexor on the left side, and the right abdominal reflex was absent while the left was brisk. In a third patient with a left-sided temporal lobe tumour the left plantar response invariably remained an extensor while the right was a flexor, and the left abdominal reflex was absent but the right was present. A post-mortem revealed in all these three cases herniation of a portion of the involved temporal lobe through the incisura tentorii, with a resulting dislocation of the brain-stem to the opposite side and pressure of it against the edge of the tentorium.

A defect of conjugate deviation of the eyes deserves special attention. Gordon Holmes has repeatedly emphasized the diagnostic importance of defective conjugate deviation to the contralateral side in tumours of the frontal lobe; it is then a result of involvement, direct or through pressure, of the frontal ocular area in the region of the second frontal gyrus. In this series of tumours defect of conjugate deviation to the contralateral side was seen in six cases. In three of these the tumour was situated in and distended the temporal pole so that it pressed directly against the frontal lobe. In the other three cases the tumour lay deep in the temporal lobe and extended towards the base and the uncus. In two of these a large cyst was found directly beneath the superior temporal sulcus; in the third there was a diffuse large tumour. These observations are of interest, as Foerster [3] succeeded in provoking in man a contralateral conjugate deviation of the eyes by faradization in the region of the superior temporal gyrus.

Another motor symptom in this series was a homolateral, contra-

lateral or bilateral tremor of the extended extremities. When present it was especially well seen in the hands when the patient held them extended in front of him, with the palms facing down and the fingers slightly separated. The tremor was rapid, fine and vibratory, not unlike that seen in paralysis agitans, although of a smaller range and finer rhythm. It could often be best determined by holding one's palm against the separated fingers of the patient's outstretched hands. During muscular rest the tremor disappears. To observe the tremor one must examine the patient repeatedly, since occasionally it comes and goes. A similar tremor was first described by Grainger Stewart [20] in 1906 as a feature of tumours of the frontal lobe; at that time Stewart said: "I have never met with similar tremor in association with tumours situated in other regions of the brain." The tremor described by Stewart is a homolateral phenomenon. In this series four cases had ipsilateral tremor, in seven patients the tremor was contralateral to the side of the tumour, and in three it was bilateral but much slower and coarser in the contralateral hand than in the ipsilateral, and suggested the unsteadiness which one observes not infrequently in asthenic patients. The rapid fine vibratory tremor on the other side resembled that seen in exophthalmic goitre.

Attempts have been made to determine the anatomical and physiological basis of this tremor. The most probable explanation is that of Schwab [19], who regards it as part of a pallidum syndrome, basing his conclusion on six cases of temporal lobe tumour, in three of which a complete pathological examination was possible. According to him the tumour, by pressing upon or invading the putamen, releases the globus pallidus and consequently the pallidum syndrome, including the tremor, results. From this hypothesis one would expect tremor of the contralateral hand, while in my series it was seen in the ipsilateral or contralateral hand, and even bilaterally. It is of interest that neither the putamen nor globus pallidus was involved directly or by pressure in any of the cases with contralateral tremor, while in two of the cases with a homolateral tremor the corpus striatum was involved. There were, however, eight other cases with extensive involvement of the lenticular nucleus in which no tremor was seen.

The contention of some authors that the tremor is due to involvement of the thalamus is untenable, since it is impossible for a temporal lobe tumour to invade the thalamus without encroaching on the lenticular nucleus and internal capsule. The fact that the tremor was seen in some cases in the ipsilateral hand, in some in the contra-

That a rough test for visual inattention is more sensitive than a perimetric examination, however expert the examiner may be, is seen from the fact that in not one of these five cases did repeated perimetric examination reveal any visual defect.

In evaluating these observations, it must be remembered that, according to psychologists, visual attention on the right side is normally greater than that on the left. The five cases (two right-sided and three left-sided tumours) with the visual inattention but negative perimetric findings, added to the sixteen cases with normal visual fields, give a total of twenty-one cases where perimetric examination was of no actual help in lateralizing the lesion. In other words, in a series of thirty-eight cases of temporal tumour, the perimeter was valuable in the diagnosis in only seven instances, or in 18.5 per cent. This result makes one doubt the validity of Cushing's statement that "the perimeter as a diagnostic aid in temporal lobe tumours is possibly the most important agent of all."

Subjective visual disturbances were of no localizing significance. There were complaints of visual disorders in eighteen cases. The most frequent symptom was failing vision, which was present in fifteen patients, and commenced on the average 3.5 months before admission to the hospital. Three patients complained of transitory momentary amblyopia, which is probably a result of rapidly progressing papilloedema. Post-mortem findings in these three patients gave no support to the opinion expressed in the literature that such a transitory amblyopia in intracranial tumours is a result of a periodical distension of the third ventricle with fluid.

Hearing.—Notwithstanding the generally accepted view that the cochlear fibres of the auditory nerves do not decussate completely, and that each auditory nerve is connected with both hemispheres, from time to time reports appear in the literature of complete deafness in the ear contralateral to the side of a temporal lobe tumour. That partial loss of hearing may accompany temporal tumours is suggested by reading carefully taken histories of such patients. Little is known of partial disturbances of hearing, because of the inadequacy of present-day methods of testing it. In this series of cases there were definite disturbances of hearing, though the ears were normal, in three patients. One with a left-sided temporal lobe tumour noticed increasing deafness in the left ear for a year before admission to the hospital, and this actually was his first symptom. Another patient with a left-sided temporal lobe tumour was aware that he could not understand simple

questions, but this was partly due to aphasia. A third patient, with a right-sided temporal lobe tumour, gradually lost hearing in both ears about two months before admission to hospital. It is interesting that the patient with the auditory sensory auræ and local motor fits had no disturbance of hearing. Three instances only, in a series of thirty-eight cases, cannot justify definite conclusions, but I believe that progressive failure of hearing in both ears, in a patient with an intracranial tumour, should, in the presence of normal cochleæ, put one on the look-out for a temporal lesion.

Disturbances of smell and taste.—The present-day methods of testing of smell and taste lack the preciseness and the objective character of the examination of vision. Most likely it is due to the defects in our tests that disturbances of smell and taste are rarely observed in temporal tumours in the intervals between epileptic fits, notwithstanding the fact that the olfactory centre is situated in the temporal lobe. Complete anosmia and ageusia hardly ever occur in uncomplicated cases. It is only when the tumour extends forward along the orbital roof and involves the olfactory tract that it causes complete anosmia.

In my series disturbances of smell and taste were observed in three patients. One patient with a right-sided tumour had a bilateral defect of smell and impaired taste. In another patient with a right-sided tumour perseveration of smell and taste on both sides was observed. In a third patient with a left-sided tumour taste was completely absent on the entire left side of the tongue, though the trigeminal and the facial nerves were apparently not involved. All the three patients were ignorant of these disturbances before examination. I have repeatedly seen in intracranial tumours, not only in those situated in the temporal lobe, a slight depression of the acuity of smell and taste, which is merely a result of increased intracranial pressure. Authors who describe disturbances of smell as a homolateral symptom and disturbances of taste as a contralateral symptom of tumours of the temporal lobe are greatly in advance of the position suggested by a study of clinical material.

Disturbances of speech.—The differentiation into different groups of disturbances of speech according to the degree of involvement of the various components of normal speech is of doubtful value in the symptomatology of temporal tumours. The type of the tumour, its position and size, the condition of the ventricular system, and finally the reaction of the surrounding brain tissue are all factors in determining varying defects of speech. It is therefore of little value to attempt to localize precisely a tumour from the nature of the speech disturbances it has

produced are full of pitfalls. There is probably more truth than error in Cushing's statement that the aphasia associated with temporal lobe tumours is a neighbourhood rather than a focal symptom. As a rule, however, the disturbances of speech produced in the early stages by tumours of the temporal lobe are of the usual types, and the most frequent symptoms are loss of power to recall words and to name objects, places and persons.

Aphasia was observed in twelve of the twenty-one cases of left-sided temporal tumour, excluding one case in a left-handed person. The disturbances of speech set in on an average five weeks before the admission of the patient to hospital, but in four cases only aphasia was the first localizing symptom. The most striking feature in one patient was inability to understand spoken or written words, and to write. In three other patients there was only a difficulty in naming objects, places and persons. In the remaining eight patients the disturbances of speech were complex. In these the first symptom was usually the occasional want of words in conversation, and then the use of wrong words, the difficulty increasing until the patient talks only jargon, his words are all "jumbled up," as the wife of one patient expressed it, he utters strings of words without meaning, and many words are of his own fabrication, frequently he is not aware of his errors. This verbal aphasia is, however, preceded by a nominal aphasia; the patient cannot recall the names of objects and persons, although later the name may come into his mind quite readily. In three cases the patient could not read, in two they were unable to write, and in two others there was definite evidence of apraxia. Defects of articulation were completely absent in all these cases.

The fact that aphasia was the most important localizing sign in only four cases out of twenty-one left temporal lobe tumours, and was present in twelve cases only, indicates that it is not, as it has been considered for long, the most prominent symptom in left-sided tumours. An analysis of the cases in which speech was normal shows that aphasia does not occur in basal temporal tumours, and that small tumours may invade the temporal lobe without disturbing it.

Much has been written on those rare cases in which aphasia accompanied a tumour of the right temporal lobe in a right-handed patient. This series includes no such case. I believe that in such cases the aphasia is due to compression against the skull of the dislocated left hemisphere, rather than to the presence of a speech centre in the right temporal lobe. I have seen a case in which left unilateral hydrocephalus

associated with a right-sided cerebral tumour produced aphasic symptoms.

Cranial nerves.—Only the first five cranial nerves come into consideration in connection with tumours of the temporal lobe. The optic and olfactory nerves have been dealt with above. Among the other four cranial nerves, the oculomotor and the trigeminus occupy the most prominent place. The topographical relations of these nerves to the temporal lobe are so intimate that it is not surprising that they often furnish important localizing signs. It is true, however, that the tumour may compress the oculomotor nerve without producing clinical signs, probably owing to the nerve being displaced gradually.

In a paper to which I have already referred, Kennedy says: "In none of these cases (nine temporal lobe tumours) was this result (partial third nerve paralysis) observed, nor was it present in the other cases of temporal tumour which have come under my observation." This statement is perplexing in view of the evidence to the contrary presented by Knapp and others. Almost forty years ago, MacEwen [12] first called attention to paresis of the third nerve in association with temporal tumours. About twenty years later, Knapp attempted to classify the various oculomotor paretic signs observed in these tumours, and since then he has repeatedly emphasized the importance of partial third nerve paralysis. While an analysis of the findings in the present series of cases confirms in the main the diagnostic significance of partial third nerve paralysis in temporal lobe tumours, I doubt the validity of Knapp's explanation of its pathogenesis.

Oculomotor palsies were observed at one time or another during the patients' stay at the hospital in twenty-one patients. Contrary to Knapp's frequently stressed statement that ptosis is the most frequent symptom, in these twenty-one cases it was observed in seven instances only, while pupillary changes were present in eighteen patients. Ptosis was observed on the ipsilateral side in four patients, in one it was contralateral and in two bilateral. The pupillary changes and the ptosis are transitory but recurring phenomena, and become persistent late in the disease.

There may be changes in the size of the pupil and in its shape; the former are more common, as in seventeen instances there were alterations in the size of the pupils and in only four changes in shape, and in three of these it accompanied changes in size.

In his studies of the symptomatology of temporal tumours, Knapp always speaks of mydriasis of the ipsilateral pupil as the most prominent

change, but a study of my material does not bear this out. Continuous observation of a patient with a temporal tumour may show at first an extremely slight myosis of the ipsilateral pupil which may be so slight that it requires repeated examination; it may remain for a day or two and then disappear, to return later in more marked degree. Finally, it becomes persistent and well marked, but as the tumour grows the pupil becomes dilated and much larger than its normal fellow, myosis gives way to mydriasis. This state persists up to the end if the disease is left to its natural course. These changes in the size of the pupil were actually followed in six patients of this series. In the others operation was undertaken before myosis gave way to mydriasis.

The fact that mydriasis appears only towards the end, and that ipsilateral myosis is the leading pupillary change in temporal tumours, has an anatomical explanation much less hypothetical than those offered by Knapp and by Mingazzini. Knapp maintains that ptosis always precedes the pupillary changes, and to explain it assumes that the fibres for the levator palpebræ are more vulnerable than the other fibres of the oculomotor nerve, and, therefore, in a slight affection of the nerve they suffer first. Mingazzini's suggestion [13] that the ptosis is of cortical origin and occurs when the superior temporal gyrus is involved, is entirely at variance with all clinical and pathological evidence.

The fact that myosis and ptosis are the only signs of oculomotor paresis and that weakness of the external ocular muscles is absent until late in the disease, and even then is extremely rare, at once suggests that they are not due to lesions of the oculomotor nerve itself. Myosis and ptosis are the most obvious components of the so-called Horner's syndrome, which is produced by a lesion of the sympathetic fibres to the head. The oculopupillary sympathetic fibres reach the base of the brain as the plexus caroticus internus along with the internal carotid arteries. There the plexus divides into two bundles; one accompanies the oculomotor nerve and the other runs to the Gasserian ganglion and joins the first division of the trigeminus. The latter fibres pass to the eye in the company of the ciliary nerves (naso-ciliary and long ciliary) and supply the dilator pupillæ; the fibres accompanying the oculomotor supply the involuntary palpebral muscles. For anatomical reasons the first division of the fifth nerve, before it disappears in the foramen rotundum, is especially liable to pressure by an enlarged temporal lobe and the sympathetic fibres loosely attached to it are the most liable to suffer from such pressure. At first this produces a paresis of the dilator

pupillæ and myosis of the ipsilateral pupil, which is transitory, since the pressure provoking it varies with the periodic disturbances of the circulation of the cerebrospinal fluid and of intracranial pressure. When the sympathetic fibres accompanying the third nerve are compressed, the involuntary palpebral muscles relax and ptosis ensues.

In my series ptosis was less frequent than myosis, and made its appearance at a relatively later date. This is readily explained by the fact that the oculomotor nerve, which is accompanied by the palpebral sympathetic nerve fibres, is less firmly fixed in its intracranial course than the first division of the trigeminus, and, therefore, responds to pressure later. On the further enlargement of the temporal lobe in the later stages of the disease, the oculomotor and the trigeminal trunks are involved by the increasing local pressure; then the sphincter pupillæ is paralysed and ipsilateral mydriasis replaces myosis.

I consequently regard the early oculopupillary changes in temporal tumours as part of an incomplete Horner's syndrome. Enophthalmos is less frequently observed, especially as it is apt to be transitory. The instillation of cocaine in the eye to determine whether the pupillary changes are due to a paresis of the third nerve or to a paresis of the oculopupillary sympathetic fibres, would be of diagnostic interest, but it was not carried out in any case of the present series.

The fact that, notwithstanding the relative frequency of herniation of a portion of the temporal lobe through the incisura tentorii and the pressure frequently exerted by the enlarged temporal lobe on the interpeduncular space, complete third nerve palsies are not seen in these cases, still further supports the explanation that the oculo-pupillary changes are due to involvement of the sympathetic fibres and not of the oculomotor. In only two cases of this series was a paresis of the internal rectus observed, and in both it appeared simultaneously with mydriasis. In these two cases no herniation of the temporal lobe through the incisura tentorii was found. On the other hand, there was no evidence of paresis of the oculomotor nerve, and a sympathetic homolateral myosis in only one, of the three cases in which pressure of the cerebral preduncles against the edge of the incisura tentorii caused a homolateral lower facial weakness, absence of the homolateral abdominal reflex, or a homolateral extensor plantar response.

It is generally admitted that absence of the corneal reflex is a most delicate index of involvement of the first branch of the trigeminus, but it is of value only in those cases where there is no hemiparesis or hemihypæsthesia of the same side. After excluding all cases of corneal

areflexia in patients with central motor or sensory disturbances there remain seven cases in which the ipsilateral reflex was diminished or lost. In one of these, in a patient with a contralateral central hemi-hypæsthesia, the corneal reflex was absent on both sides.

Sir William Gowers [4] has pointed out the fallacy of relying, in advanced intracranial tumours, upon an abducens paralysis as a localizing sign. As far as I am aware, the literature of temporal tumours contains only a single case, that recorded by Knapp, with a bilateral paralysis of the abducens. Knapp has repeatedly stated that paresis of the abducens nerve is very rare in temporal tumours. In at least seven cases of this series the sixth nerve was involved; in three the external rectus muscle was merely weak, in the other four it was completely paralysed. These disturbances were present when the patients were admitted to hospital. In five patients the paresis was unilateral, in the other two it was bilateral. When unilateral it was always on the side of the tumour. In the bilateral cases the external rectus muscle on the side of the tumour was completely paralysed, while the opposite muscle was only weak. The frequency of involvement of the abducens nerve in temporal lobe tumours would be even greater if the transient diplopia of which four other patients complained—though there was no demonstrable ocular palsy—could be attributed to a temporary weakness of an external rectus muscle.

SUMMARY AND CONCLUSIONS.

The main criticism that may be advanced on the conclusions drawn by individual writers on the symptomatology of tumours of the temporal lobe is that they attempt to establish too rigid and too definite symptom-complexes. The temporo-sphenoidal lobe is too large an area of brain for it to be possible for lesions of it, variable in type and extent, to produce any one definite train of symptoms and signs. For these reasons I shall not attempt to formulate here a definite temporal lobe syndrome, but shall merely enumerate the various symptoms and signs in the order of their frequency in this series of thirty-eight tumours of this lobe.

Headaches.—Although complained of by every patient in this series, headaches *per se* are of no localizing value. Local pain or tenderness, which was observed in ten patients (26 per cent.), is of greater value. It is frequently quite characteristic; it is a sharp, agonizing pain, comes on suddenly in paroxysms and disappears abruptly. It is probably due to local pressure on the branches of the trigeminal nerve.

Vomiting was present in 50 per cent. of the cases. It has no localizing significance and, as in other intracranial tumours, is merely a symptom of increased intracranial pressure.

Papillœdema.—Definite œdematous changes were seen in the optic discs in 86 per cent. of the cases. The comparative degree of swelling of the nerve heads on the two sides is of lateralizing value only in the incipient stages of the papillœdema.

Incontinence.—This symptom was present only in 20 per cent. of the cases. While in frontal lobe tumours sphincter disturbances seem to be a result of psychic disorders, in temporal growths they are merely a symptom of increased intracranial pressure.

Psychic disturbances.—The diagnosis of an intracranial tumour cannot possibly be made from the presence of psychic disturbances alone; however, when the diagnosis has been made from other symptoms and signs, certain psychic disturbances may help to localize the tumour in one or another part of the brain. Defects of memory were present in 50 per cent. of the cases of this series; a disturbance of memory was observed in a nearly equal proportion of frontal tumours, but it is not unusual in tumours of the temporal lobe to observe a loss of memory for both recent and past events, while in tumours of the frontal lobe it is only the recent events that are not remembered by the patient. Changes in personality, hypersomnia, and mental confusion are of little value in distinguishing between temporal and frontal tumours; they are, however, of some importance when subtentorial tumours are to be considered, for with these they hardly ever occur. The tendency to attribute psychic disturbances to lesions of the left hemisphere in right-handed people is not supported by clinical facts, and, therefore, they have no lateralizing value.

Fits.—Fits occurred in 50 per cent. of the cases, but only in 40 per cent. were they of localizing or lateralizing value. They were a relatively early symptom, especially focal sensory fits, which were observed in 32 per cent. of the cases. Uncinate fits and dreamy states are of merely localizing value, but the visual hallucinations that may accompany them are of lateralizing importance when they occur in a part only of the visual field. The visual sensations which occasionally follow closely on the uncinæ auræ are of a complex nature, and thus differ from the crude visual phenomena occurring in fits associated with lesions of the occipital cortex.

Motor and sensory disturbances.—Although obviously a neighbourhood symptom, motor and sensory disturbances were observed in 92 per

cent. of the cases of tumours of the temporal lobe. In twelve patients the whole contralateral side of the body was affected; in seven there was weakness of the arm and face only; in five a weakness of the face alone was seen; in three the contralateral arm alone was involved; weakness of the leg and face was present in three instances, and in two patients there was paresis of the arm and leg. A defect of conjugate deviation of both eyes to the contralateral side was present in six patients. In fourteen patients a fine vibratory tremor of the hand was observed, in the ipsilateral hand in five cases, in the contralateral in seven cases, and in the remaining three it was bilateral. The most constant of the motor and sensory symptoms was a contralateral lower facial weakness; it was observed in 66 per cent. of all the cases of this series. The abdominal reflex is not so important as a lateralizing sign; only in fifteen patients (39 per cent.) was it decisive on this point. A definite contralateral extensor plantar response was seen in nine patients, and in eight the response was a doubtful extensor; in other words, the plantar response had a lateralizing value in about 45 per cent. of all cases. In general, the extensor plantar response is a somewhat later sign than the disappearance of the abdominal reflex.

Disturbance of gait and balance.—The findings of this series of cases give no support to the hypothesis of the existence in the temporal lobe of an organ of balance. The so-called "pseudo-cerebellar signs" are rarely seen in temporal lobe tumours, and even when present are of no localizing or lateralizing significance.

Visual disturbances.—The mere fact that trustworthy examinations of the visual fields were possible in 74 per cent. only of the cases of this series detracts from the diagnostic importance of visual disturbances in tumours of the temporal lobe. Defects of lateralizing importance were found in only seven cases (18 per cent.). In over 46 per cent. of the twenty-eight cases with reliable examinations the fields were normal. The relative rarity of defects in the visual fields in tumours of the temporal lobe is explained by the fact that the fibres of the optic radiations, in their course towards the area striata, wind around elastic and yielding structures, the inferior and the posterior horns of the lateral ventricle.

Disturbances of hearing have little localizing and no lateralizing value, but increasing impairment of hearing in both ears in a patient with an intracranial tumour should suggest a temporal lesion, provided, of course, that the cochleæ are normal.

Disturbances of smell and taste are of no localizing or lateralizing value in tumours of the temporal lobe.

Speech disturbances.—It is obvious that disturbances of speech when present in a right-handed person assist greatly in the local diagnosis. That aphasia is not of as great diagnostic importance as one is led to believe from the literature is evident from the fact that in twenty-one right-handed patients aphasia was a definite symptom in twelve cases (57 per cent.) only, and was the first localizing sign in only four patients.

Cranial nerves.—Oculo-pupillary changes were observed in twenty-one patients (55 per cent.); eighteen of these showed pupillary changes, either myosis or mydriasis, and ptosis was present in seven patients. The oculo-pupillary changes are transitory, and recur from time to time, but become permanent late in the disease. The commonest change is in the size of the pupil; changes of shape were seen only four times. An early slight transitory recurrent ipsilateral myosis is a relatively frequent sign. It is due to involvement of the sympathetic fibres accompanying the first division of the trigeminus which innervate the dilator pupillæ. At about the same time the sympathetic fibres accompanying the oculo-motor and supplying the involuntary palpebral muscles may be involved and ptosis result. Later in the disease, when the constantly increasing pressure of the enlarged temporal lobe leads to compression of the oculo-motor trunk proper, the sphincter pupillæ becomes paralysed and myosis gives way to mydriasis. In the same way further pressure on the first division of the trigeminus may produce ipsilateral loss of the corneal reflex.

Notwithstanding the relative frequency of herniation of a portion of the temporal lobe through the incisura tentorii, and of the pressure exerted by the enlarged temporal lobe on the interpeduncular space, complete oculomotor paralysis is not seen in these tumours.

An involvement of the ipsilateral abducens was present in seven cases. In two of these cases the paresis was bilateral, but only the ipsilateral nerve was completely paralysed.

It is my pleasant duty to acknowledge my indebtedness to the members of the staff of the National Hospital, Queen Square, London, for their permission to make use of the material on which this contribution is based, and to express my thanks to Dr. Gordon Holmes for criticisms and suggestions.

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NOTICES OF RECENT PUBLICATIONS.

The Matrix of the Mind. By F. WOOD JONES and STANLEY D. PORTEUS.
Pp. 457. Honolulu: University Press Association. 1928.

The attempt to place psychology on a more scientific basis has, during the last few years, led to the appearance of several books in which the structure of the nervous system is presented from the point of view of its evolution and function, in which, in other words, the brain is treated as the organ of mind and mental phenomena are, as far as possible, interpreted in terms of neural physiology. This excellent and interesting volume, the purpose of which is to bridge to some extent the gap between neurology and psychology, is written in a charming and lucid style, and so simply and consecutively that it will be intelligible to even those who are unfamiliar with the anatomy of the brain in the ordinary sense of the term. One author has been a well-known anatomist and is now a professor of anthropology, the other is a psychologist; their collaboration has been so intimate that it is scarcely possible to detect the sections for which either is responsible, but the first 300 pages must have come mainly from the pen of Dr. Wood Jones. After preliminary chapters on the ontogenetic development of the nervous system, the evolution of the fore-brain is traced from the first rudiment of a centralized nervous apparatus, function being as far as possible correlated with the growing complexity of structure. The nature of the pallium and its relation to more lowly placed parts are then discussed in such a manner as to bring into relief the great possibilities for further advances that the appearance of this plastic organ furnished. Chapters on the conduction and integration of sensation follow, and emphasis is particularly laid on the importance of the co-ordination of sensory impressions on the development of the cerebral cortex. The parts that the pallium and the corpus striatum take in movement and the anatomical connections that make their activity possible, are fully considered, as well as the influence on movement of the labyrinths, the cerebellum and other subcortical centres. Unfortunately the author is not conversant with much of the recent work on speech and aphasia. The second part of the book, which is written from the psychological side, emphasizes again the importance of structure in attempting to interpret function. There is here and there too facile an attempt to explain Nature's purposes and unravel all her secrets; in fact, the teleological attitude of the writer is at times wearisome, but his presentation of the subject is always stimulating and instructive. Hypotheses abound, but in most instances they serve at least to illustrate or to make intelligible more fundamental facts.

The authors have produced an extremely healthy and readable volume which will afford interest and instruction to readers of every class.

Brain and Mind, or the Nervous System of Man. By R. S. A. BERRY.
Pp. 608, with 130 illustrations. New York: The Macmillan Co.
1928. Price 31s. 6d.

The author is a well-known teacher of anatomy who is also interested in psychiatry, but his book is written for the psychologist, the educationist and the social worker rather than for the physician and the student of medicine. As a textbook on anatomy it is not very satisfactory and falls below the level of many others available, for though it contains few inaccuracies and, except in the case of the fore-brain, no striking omissions, its arrangement will not give the student a clear picture of the structure of the brain as a working mechanism. Most of the illustrations are borrowed from other sources and are not particularly well selected; the description of diagrammatic drawings as photomicrographs of the cortex is an unfortunate oversight in a volume intended for the uninitiated. The attempts at the interpretation of function on both the physiological and psychological sides are open to more criticism. His main thesis is that the internuncial neurons are the physical instrument of mind, but he proceeds to the crude assumption that they are the store-houses of memory, speech, reason and thought, and constantly implies that mental capacity and quality depends merely on the number of neurons, as in the use of the term "multineuronic geniuses." Conversely amentia, of which he makes only an anatomical classification, is simply due to a deficiency of neurons. Many pages are devoted to measurement of the head as an aid in the diagnosis of mental abnormality, and several tables are supplied which may be employed in correlating the measurements obtained. Criminality, prostitution and hysteria are grouped together as symptoms of a small brain. There is also a tendency to accept uncritically unproven hypotheses and to make loose statements on function, as that pain is conducted by non-myelinated fibres, that postural tone is the special property of the autonomic arc, and that tabetic ataxia is due to the cerebellum not receiving impulses from the dorsal columns. On the other hand, much of the recent work on the physiology of the nervous system has been neglected; no reference is made to Magnus's researches in the discussion of the functions of the brain-stem, or to Pavlov in describing the activity of the cerebral cortex.

Handbuch der Neurologie des Ohres. Herausgegeben von G. ALEXANDER, O. MARBURG und H. BRUNNER. II. Band, 1te Hälfte. S. 722, mit 155 Abbildungen. Berlin und Wien: Urban und Schwarzenberg. 1928. Price M. 75.

The first and third volumes of this encyclopædic treatise on the neurology of the ear have appeared during the last five years and have been noticed in this Journal; the second volume will deal with more special subjects, and its first half, running to 720 pages, is under review. As the previous parts, it contains some matter which is only indirectly connected with the

auditory or labyrinthine apparatuses; Sträusslers' long chapter on the congenital defects, malformations and heredogenerations of the nervous system may be mentioned as an example, though this is an interesting and useful compendium on the subject for the neurologist.

The first chapter, by Pollak, deals with the affections of the facial and trigeminal nerves associated with diseases of the outer and middle ear; the second, by Spiegel, with involvement of the sympathetic system. Other chapters of particular interest to the neurologist are those on deaf-mutism by Urbantschitsch; cerebral concussion and fracture of the base of the skull, by Schönbauer and Brunner; the aural symptoms in various cerebral diseases by Alexander, and the vascular affections of the brain-stem and cerebellum by Stiefler. Sections on aural concussion, gunshot wounds of the ear, injury of the ear by changes in atmospheric pressure and vascular disease of the labyrinth, will appeal more strongly to the otologist. This part maintains the same high level of subject matter, editing and production that distinguished the previous volumes.

Kehlkopf und Rachen in ihren Beziehungen zu den Erkrankungen des Zentralnervensystems. Von B. FREYSTADTL. S. 324. Berlin: S. Karger. 1928. Price M. 17.

This textbook deals with the functional disturbances of nervous origin of the larynx, pharynx and tongue, as well as with the disorders of deglutition, respiration and articulation, that result from interference with their nervous control. In the first section the anatomy and physiology of these structures is discussed in considerable detail, and the symptoms that result from lesions of the different motor and sensory nerves that innervate them are described. This section is on the whole satisfactory, but it would have been more readable and useful if the author had been content to state his own experiences, or had collated them briefly with the views of others, but an uncritical collection of all manner of hypotheses is the usual failing of almost all such compilations. The second and larger part of the book is devoted to a description of the pharyngeal and laryngeal symptoms that form part of, or may occur in, different nervous diseases. A bibliography at the end of the book may be useful to anyone who wishes to find references to rarer laryngeal symptoms of nervous origin.

Experimentelle Neurologie (Physiologie und Pathologie des Nervensystems). By E. A. SPIEGEL. S. 281. Berlin: Karger. 1928. Price 24 M.

This volume constitutes the first part of a treatise on experimental neurology, the second half of which is due shortly to appear. While there is no lack of excellent monographs dealing with the morphology of the nervous system, there is an obvious need for a modern and comprehensive textbook dealing more particularly with physiological aspects. Dr. Spiegel's book

admirably fills this gap. In this first volume he deals with the methods of investigation which lie at our disposal; then follows a general consideration of the nature of the nerve impulse. The beginner is recommended to commence the work by reading Chapter III, which deals with the reflex activity of the central nervous system. Chapters on the segmentation of the spinal cord and its roots, and on the vegetative nervous system, complete the volume. The work is illustrated by original diagrams which are lucid and admirably drawn.

We are promised in the second volume a consideration of static and kinetic innervation, of the course of the centripetal nerve impulse, the physiology of consciousness, the circulation of blood and spinal fluid and lastly a bibliography. When completed, Dr. Spiegel's work will constitute the most important monograph of its kind.

Handbuch der biologischen Arbeitsmethoden. Abt. 5. Methoden zum Studium der Funktionen der einzelnen Organe des tierischen Organismus. Teil 5a, Heft 4. By URBAN and SCHWARZENBERG. Berlin and Vienna. 1928. Rm. 8.

This volume is a recent contribution to the exhaustive textbook on the methods of biological research which is in the course of publication under the editorship of Professor Emil Abderhalden. The following papers are contained in this particular number. "The Theoretical Basis of the Methods of Estimating the Elastic Properties of Muscle," by Steinhausen; "The Rate of Course of the Wave of Contraction in Muscle and the Speed of the Nerve Impulse," by Schiff; "Methods of Estimating the Latent Period in Muscle," by Schiff; "Kymocyclographic Methods of Investigating Movement," by Bernstein; "The Illustration of the Nerve Impulse by Means of Models," by Ebbecke. Research workers in the domain of muscle physiology will appreciate the value of these important contributions.

Organic Inheritance in Man. By F. A. E. CREW. Pp. 214. London and Edinburgh: Oliver and Boyd. 1927. Price 12s. 6d.

The subject matter of this volume is based upon the first series of William Withering Memorial Lectures delivered at the University of Birmingham. The first few chapters concern chiefly the biological and mechanistic aspects. Of particular interest to medical men are Chapters VI and VII, in which the normal and abnormal features of organic inheritance are treated. Herein the author deals in a most interesting fashion with the transmission of morphological peculiarities, and with such problems as those of sinistrality and longevity; the question of blood-groupings and their medico-legal importance in cases of disputed paternity; Manoilov's test for identification of races and twinning; these are only a few of the many problems that are considered. A special chapter is devoted to the questions of inbreeding and parental consanguinity. In the sections on the pathological aspects the various heredo-

familial affections are tabulated according to their biological characteristics—whether dominant or recessive. One may quote some of the author's practical suggestions as to a policy with regard to imbecility; the feeble-minded should not be allowed to marry into a family in which there is a history of feeble-mindedness; paupers, criminals, habitual drunkards, vagrants, prostitutes, should be examined carefully and scientifically in order that the victims of circumstance might be separated from the victims of organic inheritance and treated differently; the feeble-minded should be segregated. The author suggests that sterilization should be considered, but he points out that libido is not extinguished by this means, and hence the spread of venereal disease still remains a possibility. In the appendix there are numerous genealogical tables illustrating the mode of inheritance of various diseases, including many neurological disorders.

Dr. Crew's monograph can be recommended as a most valuable and instructive account of a difficult but fascinating aspect of medicine.

The Opium Problem. By CHARLES E. TERRY and MILDRED PELLENS.
Bureau of Social Hygiene. Pp. 1,042. New York. 1928.

This detailed and comprehensive study of the problems of morphism in all its aspects was drawn up as a report presented to the Committee on Drug Addictions. Questions of ætiology, symptomatology, withdrawal phenomena and treatment are dealt with in turn. The latter half of the volume concerns the sociological, national, state and municipal efforts at legislative control of the opium traffic. All who are interested in any aspect of morphism will find in this encyclopædic report a wealth of data, enhanced by quotations from other workers in this field. A very full bibliography completes the volume. One will not find, however, any dogmatic conclusions based upon personal experience, for the report is essentially a compilation. Such expressions of opinion as are found are purely tentative; the factors of ætiology are regarded as inconclusive, and the authors indicate the need of a carefully conducted study covering a long series of cases. With regard to the social and psychical status of the *habitues*, we read that opium addiction is not restricted to any social, economic, mental or other group; that there is "no type which may be called the habitual user of opium, but that all types are actually or potentially users." Speaking of treatment, the authors stress the ambiguous significance of the word "cure," and they restrict this term to the return of the patient to somatic and psychical integrity. Most of our therapeutic measures have not advanced beyond the stage of empiricism, and the authors deem it more desirable "to employ tentatively methods of treatment that appear to be based on such pathologic changes as are at present recognized in individual cases."

In this report we realize clearly the difficulties which have accumulated around the problem of opium addiction as the result of personal bias, the want of accurate data, and the vague impressions derived from a limited experience.

To the students of drug addiction this volume represents the most exhaustive and up-to-date *exposé* of the opium problem, and will rank with the monographs of Maier on "Cocainism," and Beringer on "Mescalism."

Langages neologiques et des Idées délirantes en Médecine mentale.

By Dr. G. TEULIÉ. Pp. 165. Paris: Auguste Picard. 1928.

Price 25 frs.

This volume is an examination of the neologisms found in the language of the insane. The object of the study was to establish whether neologisms can ever reach the stage of development into a new language, and to determine the relation, if any, between such neologisms and the ideas of the delirious flight of mania. The author, as a result of his study, concludes that neologisms and neologistic language are but degrees of one process, and that a new language in the true sense never arises in a mind with deteriorated powers. The poet and mystic alone are able to create new linguistic and coherent forms. The author attempts to give prognostic significance to the appearance and chronicity of neologisms and glossolalia, and attempts a classification. This monograph should prove of value to all who are students of the enigma of schizophrenia, but from the point of view of the study of language the material needs examining in the light of general philology. Interesting discoveries might be made.

Cours de Psychologie. By MARCEL FOUCAULE. Tome II. "*Les sensations élémentaires.*" Pp. 260. Paris: Felix Alcan. 1928. Price 20 frs.

This volume is a compilation of all the data relating to the physiology and psychology of the senses. Each sense is carefully dealt with in its physical and mental aspects, and the data gleaned from pathological states receives some attention. On the other hand, the proprioceptive system receives little or no attention, and in the chapter on sensation related to movements of the head no reference whatsoever is made to the work of Magnus and de Kleijn. This volume should prove of use to neurologists who are engaged on the careful exploration of disturbances of sensibility. Ordinary neurological textbooks are poor in such information, and it calls for laborious hunting in psychological journals to obtain all the facts which the author has here gathered together.

Stammering. A Psycho-analytic Study. By ISADOR CORIAT. Nervous and Mental Disease Monographs. No. 47. Price \$2.50.

This interesting and provocative monograph is frankly psycho-analytic, but it is none the less an interesting contribution to the problem of stammering.

On the basis of the psycho-analytic investigation of a series of cases, the author suggests not merely the causes of the disability, but the type of personality which is to be found amongst stammerers. He states that the

stammer arises at what psycho-analytic workers call the oral phase of development, that is to say, the subject's hedonic or pleasure interest is centred upon the oral zone of erotic interest which finds its satisfaction at the breast of the mother and in all processes related to the sucking reflex. Later the biting reflex grows out of this, and the pleasures of sucking and biting become interwoven. Frustration of the interest gives rise to negative attitudes towards the pleasure-producing object, the mother, and biting or aggression grows to represent the indignation felt as result of the frustration. The all-pervading pleasure experienced at the breast or oral stage gives rise to a feeling of complete satisfaction and dependence which, with the development of the personality, produces anomalies in character. If these views were expressed in terms of the conditioned reflex physiology, rather than in the picturesque and anthropomorphic language of psycho-analysis, the theory put forward would receive wider assent and more scientific criticism.

Elementary Conditions of Human Variability. By RAYMOND DODGE.
Pp. 107. Columbia University Press. Publication 10. Price \$1.50.

As regards human behaviour there are two kinds of variability: personal differences in response to identical stimuli, and individual variations in response to the same stimulus. After an extensive statistical investigation of stimulus and type of response, a series of correlations are drawn up. The most important condition is the refractory period which limits the frequency of response when stimulation is repeated above a certain critical rate, modifies the pattern of response to repeated stimuli, and facilitates the consolidation of isolated conscious events into series. Habituation varies according to the level; the knee-jerk suffers no modification over long periods of time, although there was a gradual increase in the latent period, but on the cortical level there is a decrease of latency with habituation, which is important for the study of learning processes. Rhythmic effects were noted. All neuromuscular reactions appear to be most effective in the morning, less so in the evening, irrespective of fatigue. The value of these studies for objective psychology and its industrial and educational applications is obvious.

Common Principles in Psychology and Physiology. By JOHN T. MACCURDY. Camb. Univ. Press. 1928. Pp. 280. Price 15s. net.

If there is virtue in conciliation, Dr. MacCurdy deserves well of both neurologists and psychologists in presenting this thorough discussion of the common principles underlying psychology and physiology. The battle between them has been as acrimonious as any scholastic debate between the protagonists of materialism and idealism, and in entering the no-man's land between the two opposing opinions he runs the risk of being sniped by the irreconcilables of both sides. In his discussion, however, the author keeps a firm foothold

in both camps, and exhibits a full appreciation of the advances made on both sides to solve the most fundamental problems of organic life. In the attempt to bring the apparent opposites together, he suggests a vocabulary which should become the nucleus of a common language. He sees in the Pattern Theory of physical and psychical processes a common ground for discussion. There is nothing new in the approach; we are conversant with it from the writings of Semon, and no one finds it difficult to apply it diagrammatically at least to the physiology of Pavlov and Sherrington on the one hand, or the Gestalt theory on the other. Where the phenomena of memory are concerned, however, as in the data of psychopathology, a pattern theory alone does not carry us very far. Conscious of this difficulty, the author turns back to the central problem of psychology—the nature of images. He argues, in dealing with Kohler's work on the mentality of apes, that some image function is at work to give rise to the successes following on trial and error. Only in conscious awareness can experience grow, and the awareness is carried over in mental growth through the agency of image functions. This view has, of course, been discussed from another angle by both Lloyd Morgan and Stout, under the form of "prospective reference," but where the author elaborates the thesis is in co-ordinating it with that linking conception—the pattern theory. This enables him to pass over to purely physiological fields. It is, perhaps, a little surprising that the data of embryology can explain themselves without reference to consciousness. Our knowledge of biochemical process has sufficiently advanced to permit us to understand "rudimentary memory" in a biochemical sense, and for all working purposes a behaviourist methodology still carries us along. It is only in a philosophic sense that the problem of consciousness arises. For scientific purposes the language of neurology and psychology will have to remain apart.

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Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

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SOME CONSIDERATIONS ON HEAD INJURIES.¹

BY DONALD ARMOUR, C.M.G., F.R.C.S.

THE practical interest and importance of the subject of head injuries, concerning as it does in its varied aspects almost every branch of our profession, cannot be denied. Among both surgical and neurological problems there is none which presents greater difficulties of decision than the treatment of head injuries. The great variety in the types of injury and of the disturbances of function which may occur, and the relatively greater or lesser importance of such injury according to its degree or localization, all combine to make impossible the laying down of any rule in the treatment of such cases. The treatment concerns not only the immediate recovery of these cases, but also the future condition of the patient. It should not be limited, therefore, merely to the saving of the patient's life, but it should aim at obtaining as normal an individual as before the receipt of the injury.

John Bell, writing a century and a quarter ago, thus expressed what will be my main thesis of this evening :—

“And we have this encouragement to consider the pathology in place of the anatomy of the skull, as the rule of our prognostics, that while anatomy and the enumeration and classification of fractures has led to an undue propensity to operation, the study of the living powers, and the mutual dependence of these parts, leads to a reserved, modest and rational practice—to a just confidence in the powers of Nature—to a careful and solicitous attention to all the insidious symptoms of an injured brain.”

And in our own time the same plea has been made by Wilfred Trotter, who says :—

¹ Presidential Address delivered to the Neurological Section of the Royal Society of Medicine, on October 11, 1928.

"In the case of head injuries it is of cardinal importance that diagnosis and treatment should be kept in a close and living association with pathology. In every case it is essential that the surgeon, before attempting to begin the treatment, should make a determined effort to call up the clearest possible picture of the actual conditions within the skull of the patient he has to deal with."

This injunction should be in the mind of every surgeon who may be called upon to deal with head injuries.

Unfortunately, in the past and even up to the present, the subject of head injuries in our textbooks on surgery appears in the section on "Fractures," and thus early the mind of the medical man is imbued with an exaggerated importance of the "enumeration and classification" of fractures of the skull to the detriment of a proper appreciation of the much more important part of the subject, viz., the damage, functional or organic, that the contents of the skull may have suffered. This is constantly revealed by the early insistence upon an X-ray of the skull being taken after a head injury, as if the presence or not of a fracture of the skull were the important factor in the case, and as if the result of the radiograph would be sufficient to determine by what means and methods the associated cerebral injury should be treated. Moreover, its very use constitutes at times a pitfall in the prognosis of a head injury because of the false importance attaching to the presence or absence of fracture of the skull, its absence always presuming a better prognosis than its presence. For the same reason there is a widespread lack of appreciation of the importance of so-called minor head injuries. "Minor" perhaps in the estimation of the patient and of his doctor, but so often "major" in its later manifestations and sequelæ. It is to this aspect of the subject, viz., head injury without fracture, that I wish to deal.

A general increase in intracranial pressure is the commonest result of a severe head injury. This is brought about in the first instance by reactionary œdema or hæmorrhage, or both. Later, this increased pressure may be aggravated or maintained by interference with the paths of absorption of the cerebro-spinal fluid by the swelling or displacement of the brain itself. This swelling or displacement acts first by blocking the cerebral subarachnoid spaces, and as a result the cerebro-spinal fluid collects in the basal cisterns and in the ventricles.

The enlargement of the basal cisterns forces the midbrain up, occluding the narrow space of the incisura tentorii. The swollen brain with its distended ventricles pushed up against the resistant dura inter-

feres still more with absorption, and so a vicious circle is established. Added to this, we have the direct pressure on the medulla of the fluid in the basal cisterns. The sum of all this mechanical pressure is exerted upon the blood-vessels of the brain, either locally or generally, giving rise to focal or widespread symptoms.

Such is the result at any rate of a severe injury. Can the same factors, in a lesser degree, explain the symptoms associated with or following upon a so-called minor injury?

The term "concussion," according to Trotter, should be used "to indicate an essentially transient state due to head injury which is of instantaneous onset, manifests widespread symptoms of a purely paralytic kind, does not as such comprise any evidence of structural cerebral injury, and is always followed by amnesia for the actual moment of the accident."

Two exceptions may be taken to this classical definition of concussion. Is it possible to affirm that the state is essentially transient, unless we limit the expression strictly to the unconsciousness and the immediate paralytic phenomena associated with it? Is it correct to affirm that concussion of the brain "does not as such comprise evidence of structural cerebral injury?"

How are we to explain the onset and persistence of those post-traumatic symptoms which are so often included under the misnomer "post-concussion neurosis"? Undoubtedly, they are largely the direct expression of disturbances of intracranial pressure; this disturbance being commonly in the direction of hypertension, though in some few cases hypotension has been found.

Cassasa explains the mechanism of concussion as depending upon the existence of "a network of fine fibrils connecting the external wall of the blood-vessels with the surrounding brain tissue across the perivascular lymph spaces." It is conceivable that any sudden overfilling of the perivascular lymph spaces with cerebro-spinal fluid could produce laceration of a vessel by the tearing of its wall in the neighbourhood of such a fibrillar attachment.

On the other hand, without such an attachment the laceration of a vessel surrounded by fluid could not be produced by any pressure exerted through that fluid, which would tend to compress the vessel but not to lacerate it. Such an increase of cerebro-spinal fluid in the perivascular lymph spaces could be caused by the cerebro-spinal fluid from the surface of the brain being driven into it by the pressure exerted by the change of shape of the skull as the result of a blow or a fall.

This change of shape under an area of violence is in the direction of flattening and diminution of space for the cerebro-spinal fluid in that area. This fluid must find its way out of that area through the various sulci of the brain, and such fluid as cannot find its way through these channels must find a way into the perivascular lymph spaces in the reverse direction of the normal flow of the fluid in these channels. Now Weed's experiments have demonstrated that the perivascular lymph sheath—the Virchow-Robin space—is directly connected with the finer spaces about the central ganglion cells.

Cassasa suggests that sudden physical distension of these periganglionic spaces by cerebro-spinal fluid in cases of concussion causes a direct physical change in the ganglion cell, which may explain all the phenomena of concussion of the brain. He thinks these simple changes may occur without minute hæmorrhages, and explains the completely negative findings at post-mortem examination in many cases of concussion.

Osuati and Giliberti go further in emphasizing the structural factors in concussion of the brain. Basing their opinion upon the study of 100 cases of concussion, they conclude that not only is there actual cerebral injury in concussion, but in a few instances complete resolution does not occur, and that there is a strong likelihood that secondary degenerative changes develop. They suggest the term "traumatic encephalitis" in place of "post-concussion neurosis."

Whether these engaging theories are capable of proof, or not, there can be no doubt that the symptoms usually following concussion—the commonest of which is headache of varying quality—are the expression of an altered pressure of the cerebro-spinal fluid. Not only a stable alteration in pressure in one or other direction, but an instability of pressure such as has been described in epilepsy, would seem to be the cause in a certain number of cases.

Mestrezat, Bouttier and Logre found in 80 per cent. of a large number of cases of concussion without head wounds definite changes in the cerebro-spinal fluid. The essential features were an increase in tension and an excess of albumin, while the chlorides were normal, the sugar rather increased, fibrin absent and the permeability normal. The interpretation placed by them upon such a fluid was that it was due to an aseptic disintegration of nerve tissue without meningeal involvement, combined with a marked tendency to hypersecretion.

This "formula of concussion" is also characterized by its evolution, the excess of albumin usually appearing at the end of two to three days,

and disappearing as a rule at the end of some weeks or months with return to normal. Sometimes there was an indefinite persistence, or a slow regression of the syndrome during a number of months.

They would use this "formula" for the diagnosing of an "associated concussion" in cases when no evidence of a head injury was adduced, but at the same time they would not exclude concussion owing to the absence of an anomalous cerebro-spinal fluid. A caution, however, is necessary in cases of associated nerve contusion giving the additional signs, more or less marked, of a meningeal hæmorrhage. From a medico-legal point of view, the possible imitation of their formula in syphilis of the nervous system is of the greatest importance, calling for a Wassermann test in cases showing a lymphocytosis, however slight.

In confirmation of these findings, Claude, Lamache and Dubar have lately carried out similar investigations on the cerebro-spinal fluid of patients who had suffered from head injuries without fracture of the skull. Very few of them had total loss of consciousness. The time intervening between the receipt of the injury and the examination of the fluid varied from two or three weeks to several months. These patients sought relief on account of such subjective symptoms as headache, dizziness, weakness, insomnia, tinnitus aurium and visual fatigue. Increase in albumin was found in nine out of the twenty-two cases examined, the excess tending to disappear gradually as the symptoms subsided after repeated lumbar puncture. Otherwise the fluid showed no chemical nor cytological abnormality. But the tension of the cerebro-spinal fluid was found altered in all the cases except five. The alteration took the form of hypertension, hypotension or instability of tension, the first being most frequently found.

What explanation can be offered for such alterations in the tension of the cerebro-spinal fluid following head injury? Obviously the increase following immediately upon a severe injury, with associated œdema or hæmorrhage, or both, is due, very largely at any rate, to mechanical causes. These have been described already.

The increase in tension following upon slight injuries and maintained over a considerable period may be due to such factors, acting alone or in combination, as:—

- (1) Increase in the amount of cerebro-spinal fluid secreted.
- (2) Interference with its circulation and absorption.
- (3) Variations in volume of the cranial contents, nervous, ventricular and vascular.

Granting that the choroid plexuses are the chief source of the cerebro-spinal fluid, whether the process be a secretion or a transudation, or, according to Mestrezat, a mere dialysation from the blood, can we find any conditions associated with or following upon cerebral trauma which will activate or inhibit this process?

THE EFFECT OF TRAUMA UPON THE CHOROID PLEXUSES.

The system of the ventricular cavities and their contained cerebro-spinal fluid has been said to be of importance in determining the distribution of force within the skull. The position of the choroid plexuses would thus render them particularly vulnerable, and expose them to the direct action of the wave of repercussion at the time of the accident. Can such trauma, if it occurs, affect their secretory activity?

Some writers would invoke an altered fluid, following upon microscopic vascular and nervous lesions and meningeal irritation, as being the cause of a secondary or reactionary hypersecretion.

Duret thinks that trauma causes a cerebro-spinal shock, giving rise to disturbances of the cerebro-meningeal circulation, tending to a congestion of the brain mass and producing intracranial hypertension by lessening the cranial space, by venous stasis and by augmentation of the circulation with increased flow of blood to the secretory organs, i.e., the choroid plexuses. In addition, he postulates an irritation of the meninges, ependyma and plexuses by the waste products of disintegration in cases of minute pial hæmorrhages and of post-congestion extravasations, a selective poisoning as regards function by the products of breaking-down nerve tissue as a result of microscopic tears and contusions. In short, he would attribute hypertension to hypersecretion of cerebro-spinal fluid.

The causes of hypotension are equally hypothetical. Apart from that due to the loss of cerebro-spinal fluid from trauma, following lumbar puncture and at operations, all of which give rise to a sudden hypotension, there remain the occasional cases following head injury, in which the hypotension manifests itself, usually at a later date, by definite clinical symptoms. These may be, according to Leriche, intense frontal headache, dizziness, nausea, sometimes convulsive phenomena, stupor and even coma.

In head injuries, Leriche would explain the hypotension as due to the formation of a porencephalic cyst on the surface of the brain, a

sort of supplementary sub-arachnoid cistern, resulting in a relative insufficiency of cerebro-spinal fluid and a consecutive hypotension. Most probably several factors may be responsible, such as a functional disturbance of the regulating centre of fluid tension, inhibition of the cells of the choroid plexuses, or local modifications of the cerebral circulation.

Förster and Wartenberg have called attention to certain changes in the shape and position of the ventricles following upon head injuries. These changes were chiefly in the nature of a distension or dilatation of one or both lateral ventricles, with a stretching of their summits in an upward and outward direction. The dilatation was usually greater on, or confined to, the side of the lesion—hydrocephalus internus lateralis—and the ventricle was drawn up towards the site of the lesion—"Ventrikelwanderung." This unilateral appearance may be met with in the absence of unilateral clinical findings. According to Förster, this wandering of the ventricle takes place slowly and gradually. The final result is a thin membrane comprised of arachnoid, pia and the remains of the cortex covering a dilated ventricle, which he calls a traumatic porencephaly.

Wartenberg describes as an end-result of *commotio cerebri* a condition characterized by numerous areas of hæmorrhages or softening, a persistent and progressive cicatricial shrinkage of the whole brain and an alteration in the shape of the ventricle, the latter dilating at the expense of the brain substance (passive hydrocephalus). He describes the whole brain as being drawn from its central position towards the side of the lesion—"Gehirnwanderung."

This passive hydrocephalus may be converted into an active one by a traumatic meningitis serosa ventriculi, causing an irritation of the choroid plexus with an increased secretion of cerebro-spinal fluid.

Both these authors make a plea for the routine use of ventriculography (encephalography) in late cases of head injuries, particularly if operation is contemplated. Several of their cases are reported as being very greatly improved as a result of the ventriculography alone.

Block and Oppenheimer have made a comparative study of the intraspinal pressure, blood pressure and intra-ocular pressure in head injury. In eleven cases of fracture of the skull, although the blood-pressure was below the average, the spinal pressure was above normal and the ocular pressure was above the average. They conclude that "no individual parallelism exists between intraspinal pressure, arterial pressure and ocular tension," but on an average a high pressure of one

type is associated with a high pressure of the other types; the same is true of low pressure.

Any attempt to estimate clinically intracranial pressure in the light of general blood-pressure findings is not of practical value. The presence of initial shock following a severe head injury and lasting for some hours, associated as it is with a fall in the general blood-pressure, will mask the true intracranial condition. Again, the intracranial pressure must reach a very dangerous stage of compression before it can affect the general blood-pressure in the direction of any marked increase.

Both in the acute and chronic stages of a head injury the value of the determination of the pressure of the cerebro-spinal fluid is beyond question. The estimation of this pressure to be of any accurate value must be made with a manometer. Attempts to estimate the pressure by counting drops per unit of time, or by the force with which, or the distance to which, the fluid spurts, are equally fallacious. Too many extraneous factors may be the cause of invalidating such conclusions.

It has been said that "normal pressure may be almost anything," and it must be admitted that normal pressure has certainly a wide range. Ayer places a normal pressure between 100 and 200 mm of water, regards as "suspiciously high" pressures between 200 and 250 mm., and as "definitely abnormal" those between 250 and 300 mm. Pressures over 300 mm are always to be explained on the basis of intracranial pathology.

The presence or absence of blood in the cerebro-spinal fluid following head injuries is often stressed beyond its true clinical significance. Its presence is only of importance as a corroborative sign of intracranial injury associated with bleeding from an intradural vessel. Its absence, however, does not exclude intracranial hæmorrhage, even be it subdural or subarachnoidal. From the point of view of treatment, neither the presence nor absence of blood in the cerebrospinal fluid has any importance whatever. The *pressure* of the fluid as an indication of the degree of intracranial tension is the all-important matter.

The eyes in head injury.—Immediately following upon the receipt of injury, the pupils are more or less dilated, depending upon the degree of the initial shock, and their reaction to light is correspondingly sluggish. During unconsciousness both these conditions are increased. As the stage of shock passes off the pupils usually return to their normal size and react to light, unless there be a definite increase in intracranial pressure, when the dilatation and sluggishness may remain. The pin-

point pupil in the early stage of a supracortical hæmorrhage or œdema passes into dilatation as the stage of irritation passes into the paralytic stage.

Injury to cranial nerves occurs in about 12 per cent. of head injuries, usually in basal fractures. The order of frequency would appear to be the seventh, sixth, eighth, third and second, the remaining ones being rarely involved. The frequency of combined involvement is not very great; the nerves lying close together are usually involved (seventh and eighth; second, third, fourth and sixth) by single fissure fractures; while in multiple fissures the groups, both as to the nerve involved and the side affected, are very irregular.

Varying conditions are concerned in the production of these paralyses of the cranial nerves. Probably the most frequent cause is injury of the nerve by bony compression, more rarely by laceration from displacement of the walls of the foramen. Where there has been no bony displacement, injury by bruising or laceration of the nerve sheath, with more or less severe reaction, may have occurred. Certain cases are possibly due to compression from a meningeal hæmorrhage.

But I wish to refer more particularly to the effect of increased intracranial pressure in the production of cranial nerve symptoms, more especially papilloedema, or perhaps more correctly "papillary stasis," as French neurologists call it. Cushing and Bordley some years ago showed by experiment how rapidly a retinal œdema may be made to appear in association with certain forms of increased intracranial tension, particularly when the compression is brought about by the introduction into the cranial cavity of fluid under tension; and how rapidly also the œdema may disappear when relief from tension has been afforded.

In practice it should be remembered that great assistance in estimating the grade of intracranial tension may be obtained by an examination of the fundi, for in head injuries with increased tension there may be a degree of papilloedema proportionate to the severity and duration of the intracranial symptoms.

Early signs are dilatation of the retinal veins with venous stasis, and œdema not sufficient to be described in terms of diopters. But with increasing tension there occurs an œdematous blurring of first the nasal margin and then the temporal margin of the disc, followed even by obscuration of the whole disc. As would be expected, fractures beneath the tentorium cause these changes more rapidly than those elsewhere. It is unusual, however, for these changes to appear within the first six hours.

In cases of local compression, but not when the tension is equally raised in all parts of the cranial cavity, the examination of the discs may be of great aid in determining the side on which the primary focal compression is being exercised. This unilateral intracranial stasis may have confirmatory evidence in the condition of those extracranial vessels which empty into the cranial sinuses, as shown by a dilatation of the vessels of the scalp, forehead and eyelids, and even a slight degree of exophthalmos.

Pidoux, in his study of increased intracranial tension present some time after the receipt of the injury, calls attention to the frequent occurrence of a bilateral papillary stasis, which is independent of any basal fracture or compression by effusion. With the relief of the tension the discs return to normal.

Turning to the more practical side of my subject, I would make a plea for the more frequent use of lumbar puncture as a therapeutic measure in both acute and chronic head injuries. I do not think its value is very generally appreciated. While in no way a substitute for a decompressive operation in cases of high intracranial tension, and even dangerous in some cases owing to the risk of medullary compression at the foramen magnum, in milder cases of increased tension the slow withdrawal of fluid, repeated if necessary, is of very great value. It very often allows the postponing of an operation until all the conditions are suitable, or even dispensing with it altogether. But the pressure of the fluid, not the quantity withdrawn, is the determining factor as to the further conduct of the case.

Again, in cases obviously not requiring the major operation of decompression, but suffering from severe headache, extreme restlessness, irritability, vertigo, etc., repeated lumbar puncture is of the greatest value in mitigating or curing these distressing symptoms. Therein lies the value of the so-called "spontaneous decompression" in fractures of the skull, with leakage of cerebro-spinal fluid. A value, unfortunately, too often offset by the ever-present danger of infection.

We owe to Weed and McKibben the knowledge that it is possible to lower the cerebro-spinal fluid pressure by the intravenous injection of hypertonic solutions, and conversely to increase the brain mass as well as the intracranial pressure by using hypotonic solutions. Haden, using a concentrated glucose solution, was the first to apply this knowledge clinically, while Cushing and Foley showed that the same results, though less pronounced, could be obtained by oral or rectal administration, which caused less disturbance of respiration and circulation.

Foley and Putnam believe that the decrease in intracranial tension is not due solely to decrease in brain volume, but primarily represents "new ratios between secretion and absorption of cerebro-spinal fluid."

Weed and Hughson, as a result of more extended experiments, conclude that, while the normal cerebro-spinal fluid pressure is partially dependent upon cerebral venous pressure and to a lesser extent upon cerebral arterial pressure, it is for the most part independent of either. And further, that the alterations in cerebro-spinal fluid following intravenous injection of hypertonic solutions, while partially parallel to the variations in cerebral arterial and venous pressures, are mainly independent of them and show much more marked depressions.

Fay found that the intestinal instillation of magnesium sulphate was almost twice as efficient as sodium chloride for the reduction of intracranial pressure. He attributes this to the fact that magnesium sulphate is non-dialysable, while sodium chloride is readily dialysed. He also points out that the administration of sodium chloride may produce a secondary wave of oedema and increased intracranial pressure, due to its absorption and immobilization in the tissues, with a subsequent attraction of fluid from the blood-stream. Fay calls attention to the fact that over-dehydration is possible and may be serious, if not fatal.

Howe has undertaken a series of experiments with the object of determining what solutions were least toxic and most efficient in lowering intracranial pressure when given intravenously. He tested a dozen hypertonic solutions; some were found too toxic and others relatively ineffectual. He found that sodium chloride produced the most pronounced decrease in intracranial pressure of any substance used, but is toxic unless administered very slowly. He, however, regards it as unfit for general clinical administration, on account of its immobilization in the tissues producing a secondary wave of oedema.

He found that dextrose is absolutely non-toxic and never resulted in the slightest disturbance of respiratory or cardiac action, no matter how much or how quickly it was given. 50 c.c. of a 100 per cent. solution given in less than a minute had no untoward action. He concludes that "dextrose is the only substance of this group which is non-toxic and produces a satisfactory fall in intracranial pressure."

The practical application of these measures for the relief of increased intracranial tension, whether in acute or chronic head injuries, is too obvious and too well known to require further comment.

Turning to the subject of surgical intervention in acute injuries we

are met with the problem of deciding, first whether an operation is advisable, and secondly, if so, when it should be performed. In about two-thirds of the cases of head injury there is little or no increase of intracranial tension and consequently no operation is indicated. In a certain number of others the injury has been so severe that the initial shock is combined with a rapidly appearing medullary oedema and collapse, making surgical intervention not only useless but reprehensible. We are left, however, with a remaining group in which only careful and repeated observations can determine what course we should pursue.

It may be said at once, and I desire to lay great stress upon this point, that no operation of any kind should be performed whilst the patient is in the condition of severe initial shock. It increases that shock and takes away whatever chance the patient may have had of recovery. All efforts should be directed at first to the treatment of the shock along the well-recognized lines. Again, should the patient have been allowed to pass into the terminal stage of medullary oedema and collapse, shown clinically by respiratory paralysis, with rapid and irregular cardiac action, widely dilated pupils, profound coma, complete muscular relaxation and a permanent fall in blood-pressure, no operation should be performed. These patients die, operation or no operation, and intervention only brings surgery into disrepute.

On the other hand, merely because of the absence of the usual and classical signs of fracture of the skull (bleeding and leakage of cerebro-spinal fluid from the ears or nose, subconjunctival hæmorrhages, &c.), and a negative radiograph in the presence of a greatly increased intracranial pressure, not to advise an operation is equally to be condemned. However, in the absence of such an increase of intracranial pressure; the presence of cranial nerve paralyses, of acute paralytic conditions and of convulsions, unless of a severe and persistent character, is not an indication for operation.

The ideal period for surgical intervention in acute head injuries is the "stage of capillary anæmia," when the increasing cerebro-spinal fluid pressure approximates to the capillary pressure. This stage is shown clinically by a slow pulse and a slight rise in the general arterial blood-pressure due to stimulation of the vasomotor centre. The increasing venous stasis is shown by severe headache, restlessness and even, delirium, and a definite cyanosis appears. On ophthalmoscopic examination the retinal veins are seen to be large and dilated, with or without oedema of the discs. The pressure of the cerebro-spinal fluid as measured by the manometer will be 300 mm. or higher. It may be

added here that it is of the greatest importance to observe whether the degree of coma varies with the variations of the cerebro-spinal fluid pressure. Operation in the stage of capillary anæmia should be undertaken with a view to forestalling the onset of the major symptoms of medullary compression.

This operative procedure takes the form of a right subtemporal decompression. It has several advantages due to its anatomical relations. The squamous portion of the temporal bone is the thinnest part of the vault of the skull, and as such the easiest of removal. Its removal exposes the middle meningeal artery. The most important advantage, however, is the fact that the part of the brain lying beneath the decompression opening is the temporo-sphenoidal lobe, a "silent" area. In addition, it allows of the drainage of the middle fossa of the skull at its lowest point.

The simplest operation is performed by means of a horseshoe-shaped flap, which is turned down by an incision which commences above and behind the external angular process of the frontal bone, is carried along just below the line of the temporal crest, and curving downwards ends just behind the top of the ear. This flap should include everything down to the bone. The skull is trephined over the squamous part of the temporal bone, and the bone of the temporal fossa removed forwards, backwards and downwards. The dura is then opened, any branches of the middle meningeal artery being secured and ligatured. A drain of rubber tissue, or one-half of a split tube, should be inserted along the floor of the middle fossa of the skull between the dura and the brain. The dura is left widely open. The drain should be left in for forty-eight hours or longer as the case demands. The scalp flap is sutured into place by interrupted silkworm-gut sutures.

HISTOPATHOLOGICAL CHANGES FOLLOWING MALARIAL TREATMENT OF GENERAL PARALYSIS.¹

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THE unspecific treatment of general paralysis by the inoculation of malaria, initiated by Wagner-Jauregg in the Vienna clinic, has justly led to renewed hopefulness in the combating of this disease. The very widespread adoption of this method, and the equally widespread favourable clinical results, give adequate attestation to this. That there are some disadvantages is well known, but certainly they are insignificant in comparison with the benefits derived.

At the moment the problem of greatest importance unquestionably is: What changes, following the introduction of the malarial parasite, take place in the organism that can bring about such improvement? To understand this obviously means considerable progress in the treatment, whether in the more effective employment of this method or of some other measure.

The first studies of this nature were reported in 1923 by Sträussler and Koskinas [36] on material from the Vienna Clinic. They presented the histological findings in seven cases. In four cases, in which the patients died during or directly after the treatment, the infiltration and proliferative changes in the vessels and glia were the most marked; the meninges were strongly infiltrated, macrophages being unusually numerous; the cortical blood-vessels likewise showed considerable infiltration; the infiltrative elements breaking into the nervous tissue itself in one case, and there was marked capillary and glial proliferation. On the other hand, in the three patients dying in remission there was surprisingly little change; the cortical architecture did not appear greatly disturbed, infiltration was very slight and the glia very little proliferated. They concluded that malaria leads to an increased intensity of inflammation, and that all defensive mechanisms of the central nervous system are

¹ From the Anatomical Laboratory (Professor Dr. A. Jakob) of the University Psychiatric Clinic, Hamburg-Friedrichsberg (Director Professor Dr. Weygandt).

mobilized against the noxus of the syphilitic disease. If the outcome is favourable then there is a recession of inflammation and the degenerative component of the paralytic process comes to a standstill—the picture of “stationary paralysis.”

In 1925 the same authors [37] discussed the histopathological findings in thirty-one additional cases and extended their conception of the process to include a qualitative change, suggesting that the malarial treatment not only causes an increase in the intensity of the inflammatory reaction, but that the characteristic unspecific diffuse and malignant inflammation of general paralysis (Jakob [15]) is at least partially replaced by granulomata, a more specific and benign form of inflammation. This would indicate a favourable change in the reactive ability of the body.

In 1925 Kirschbaum [20] published his findings in twenty-two cases. In those terminating during and within two weeks after treatment he found, for the most part, moderately severe general paralytic changes, though in two there was very severe infiltration and in three very slight. In those terminating after a month the infiltration was slight. In a patient dying in a remission the state corresponded to “stationary paralysis.” No convincing evidence was found of a change in character of the reaction. In only two cases were miliary gummata present.

In 1926 Gurewitsch [6] reported on twelve cases. In four patients, dying within three weeks after treatment, the changes were typical of general paralysis, and were of the severest degree. In the other eight, dying from three weeks to eight months, the changes were only moderately severe so far as the cortex was concerned, but in three there was marked infiltration of the striatum.

Among the cases examined by Nakamura (27) in 1926 are two of general paralysis which died during treatment and sixteen days after treatment respectively. In the first the paralytic changes were very severe, in the second of moderate severity. In general he was impressed by the prominence of lymphocytes and by the glial proliferation.

The findings in fifteen cases by Freeman [5] in 1927 were much the same as those of Sträussler and Koskinas. In cases examined within a few weeks of the first rigor he found a striking exaggeration of the usual paretic process, and was particularly impressed by the prominence of mesodermal proliferation. Later the picture gradually approaches the normal.

In contrast with practically all earlier findings are those of

Lehoczky [23] in 1927. He reported eleven cases treated with milk or malaria, or with a combination of the two. Of the six patients treated with malaria alone, one developed no fever and so must be excluded. One patient died fourteen days after treatment, the others during treatment. In only one case did he find intense infiltration of the cortical vessels, which in areas showed a very strong mesodermal proliferation. Another case showed similar changes confined to the left putamen. The remaining cases presented merely mild parietic changes. He thus believes that the favourable influence of malaria cannot be explained through an exaggeration of the inflammatory reaction as concluded by Sträussler and Koskinas, but rather that it causes a decrease of inflammation. He also found no evidence in support of Nakamura's claim of a change in quality, a relative increase of lymphocytes.

That some histological change takes place in the brain following inoculation by malaria seems beyond doubt, as judged by these reports, but as to the real nature of this change there is some lack of accord. Nor is it surprising that one should find considerable inconsistency in the histological picture. It is common knowledge how much at variance different cases of untreated paresis may be, and yet each possesses certain features which, when taken together, almost invariably permit a diagnosis to be made. However difficult, or even impossible, it may be to determine accurately from a few cases just what alterations may be due to the malarial treatment, it is not too much to presume that with the gradual accumulation of material certain features may become impressive by virtue of their constancy or their frequency. It is possible thus that the forty-seven cases of this report may offer some further evidence as to the nature of this process.

To follow such alterations through the various phases seemed possible only by grouping the cases according to the interval between treatment and death, and by constructing the largest possible groups so that the variations to be expected in the different cases might not obscure such features they might have in common. The following report attempts no detailed description of all the findings, but rather seeks to bring out the most characteristic changes at different intervals after treatment so that the process may be followed through its successive stages.

First, I shall consider only the thirty-eight cases that have run a clinical course fairly typical of paresis and in which the diagnosis could be verified histologically. For the above-mentioned reasons I shall describe these cases, all treated with tertian malaria, except where indicated, as follows:—

- (1) 7 cases, death during treatment.
- (2) 6 cases, death four to fourteen days after treatment (one patient inoculated with tropical malaria).
- (3) 3 cases, death three to six weeks after treatment.
- (4) 5 cases, death three to five months after treatment.
- (5) 4 cases, death six to nine months after treatment (one patient inoculated with quartan malaria).
- (6) 10 cases, death one to two and a half years after treatment (one patient inoculated with tropical malaria).
- (7) 3 cases, death three to five years after treatment.

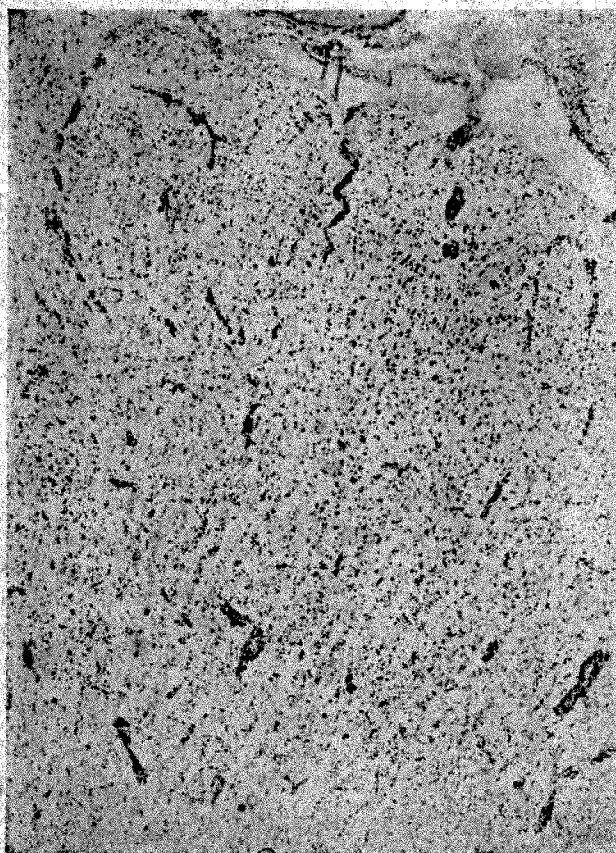


FIG. 1.—Nissl stain. Agranular frontal area. During treatment. Showing the strong and very diffuse infiltration characteristic of this period.

Group I.—SEVEN CASES TERMINATING DURING TREATMENT.

Clinical.—One patient, after having three typical rises of temperature, developed a step-like rise of fever lasting until death from "heart failure" three

days later. Four patients had eight, the other two eleven, rises of temperature. One patient developed pneumonia after the eighth elevation of temperature, and died the same day. The other patients died of "heart failure."

Histological.—The meninges are rather strongly infiltrated with plasma cells and lymphocytes, with a considerable predominance of the latter. There are also numerous mononuclear cells with varying amounts of cytoplasm in which one often sees small vacuoles and pigmented granules. These cells may be regarded as macrophages.

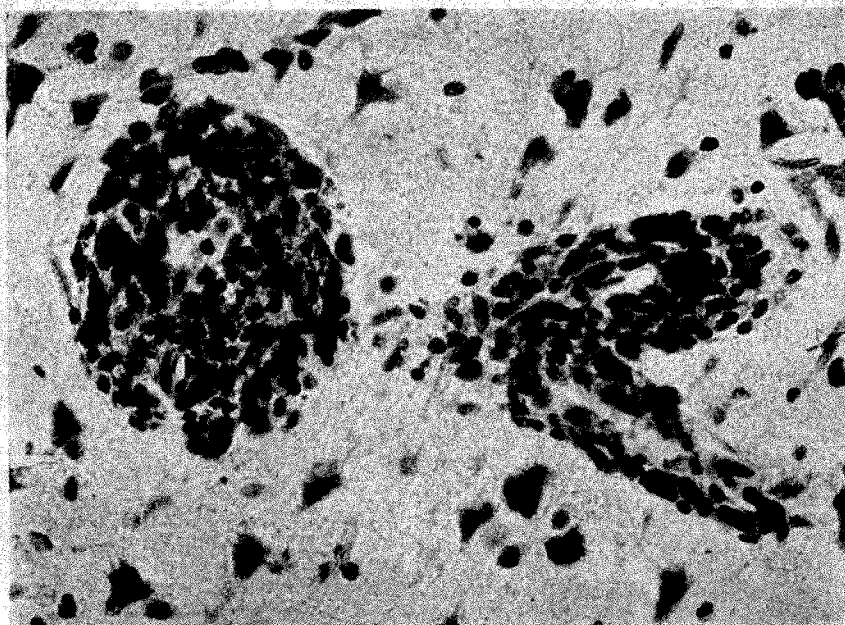


FIG. 2.—Nissl stain. During treatment. The more unusual findings of this period—vessels with considerable mesodermal proliferation.

The cortex shows a quite typical histological picture of paresis, but the reaction is rather more intense than that found in the average case (fig. 1). The infiltration is very diffuse. Practically every vessel, large and small, has its mantle of plasma cells and lymphocytes with, as is usual, predominance of the former. In some instances the cells have broken the confines of the adventitial spaces and lie free in the tissue.

No impressively strong mesenchymal reaction is present, but in occasional vessels the mesenchymal tissue is somewhat more proliferated than usual (fig. 2), or a very thick ring of infiltration composed almost exclusively of lymphocytes may be found. At times there is considerable narrowing or even closure of the lumen of the vessels, or, rarely, even small inflammatory foci near them (fig. 3). Such exceptional findings, however, can scarcely be regarded as a real qualitative change in the reaction.

The macroglia is greatly proliferated, possessing large nuclei rich in chromatin and an increase of protoplasm. The microglia is even more proliferated, the nucleus being long and rod-shaped, as is usually found in paresis. The reaction in both the walls of the blood-vessels and in the microglia is very strong. The architecture of the cortex is markedly disturbed, so that it is often difficult to recognize the several layers. The changes in all groups of ganglion cells are so nearly alike that there appears no reason for discussing them

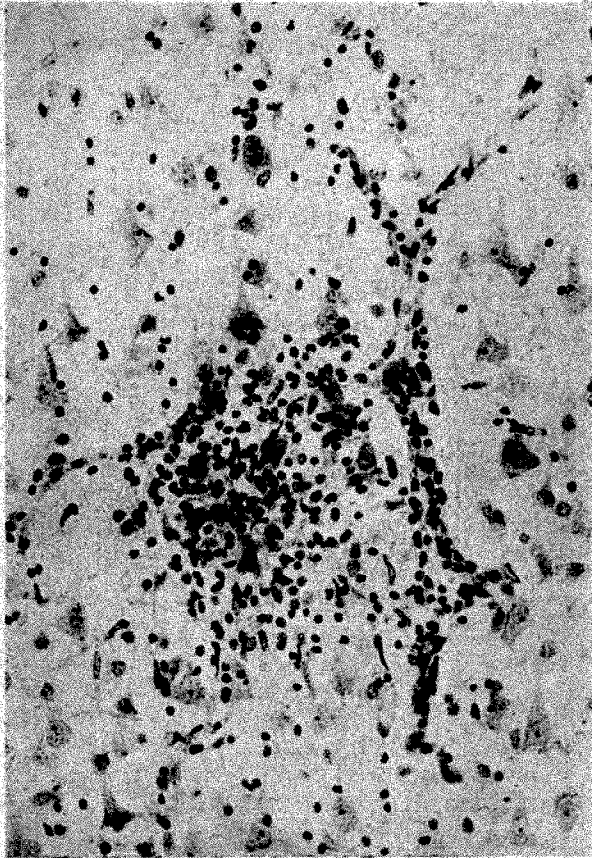


FIG. 3.—Nissl stain. During treatment. An inflammatory focus near a small vessel, such as may rarely be found.

further, much less for giving separate descriptions in the different cases, or even in the several groups. Even the cases in which there is considerable restoration of the arrangement of the cortical layers and of the nerve cells also show severe alterations in the ganglion cells.

Fig. 1 represents the type of reaction characteristic of the cases dying during

treatment. This may be summarized as an increase in intensity of the usual general paralytic reaction. No spirochaetes were found.

Other findings which do not characterize the cases of this period, but which may deserve mention for the sake of more complete description, can be briefly summarized.

The degree of meningeal thickening varies considerably in the different cases, not only at this period but in all cases. There is, however, no evidence that it is influenced by the treatment, and so it may be left out of further consideration. In addition to the meningeal infiltration already mentioned,

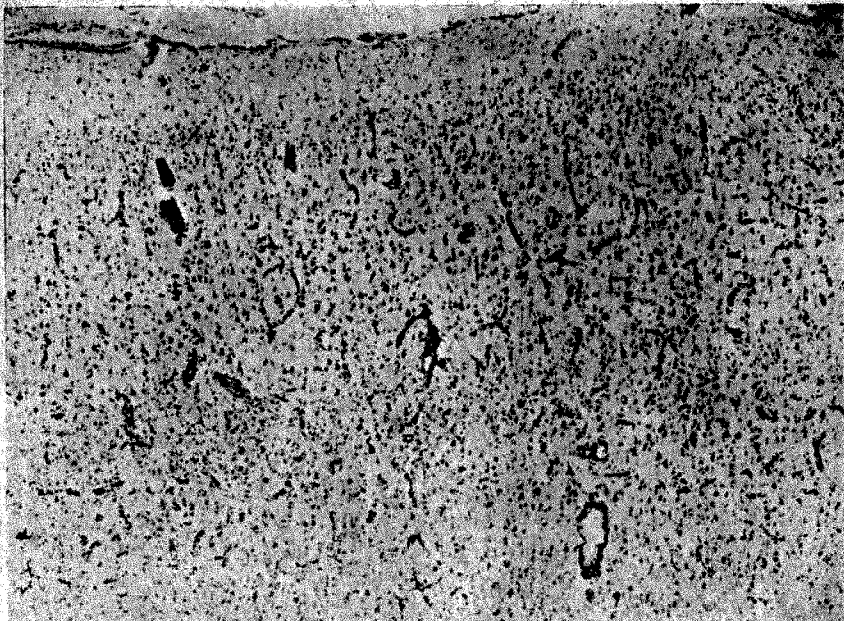


FIG. 4.—Nissl stain. Temporal lobe; seven days after treatment. The intense diffuse infiltration is still to be seen.

there are, in one case, great numbers of mast cells and degenerated plasma cells (mulberry forms). In another case many Russell's bodies are present.

In some cases degenerative changes of the walls of the blood-vessels are found. In one case, for example, an occasional vessel shows a moderate degree of intimal thickening and proliferation of the endothelial cells. In another, one fairly large cortical blood-vessel was found with thickened intima and splitting of the internal elastic membrane. Here and there are vessels with hyaline changes or deposits of chalk. The occasional thick perivascular lymphocytic rings, the less common vessels with considerable mesodermal proliferation and the rare inflammatory foci lying near the blood-vessels, have already been mentioned (figs. 2 and 3). In one case considerable blood-pigment is present in the perivascular spaces.

In some cases glial rosettes are found in the white substance, which unquestionably indicate degeneration of fibres. Jakob [14], in his study of secondary degeneration, has described in detail the relationship of glial rosettes to fibre degeneration. Such findings, however, so far as my observations go, bear no relation to the malarial treatment.

Group II.—SIX CASES. FOUR TO FOURTEEN DAYS AFTER TREATMENT.

Clinical.—One patient had a few slight convulsive attacks following treatment and later developed pneumonia which led to death. The others became



FIG. 5.—Nissl stain. Granular frontal area; three weeks after treatment. A case showing the most marked accumulation of infiltration on the small blood-vessels. This indicates the recession of the diffuseness; the capillaries are less strongly infiltrated.

increasingly demented, dying usually in a state of marasmus, some with decubitus. One patient had only three rises of temperature, the others from six to twelve.

Histological.—In this period the changes are even more severe. The meningeal infiltration remains practically the same as during treatment except for a rather striking increase of macrophages. In the cortex the perivascular infiltration has become yet greater. Here, as in the first group, plasma cells predominate and the infiltration is still very diffuse, but it differs in that somewhat thicker cell rings on the venules and arterioles are more frequent (fig. 4). The macroglia is more strongly proliferated, the microglia to practically the

same degree as in the previous groups. The iron content of the blood-vessel walls, as well as of the microglia, manifests some further increase. The disturbance of cortical architecture remains essentially the same.

In one of these cases I was able to find spirochaetes, but otherwise this case did not differ from the others of the group except for the presence of a great number of Russell's bodies ("colloidal plasma cells").

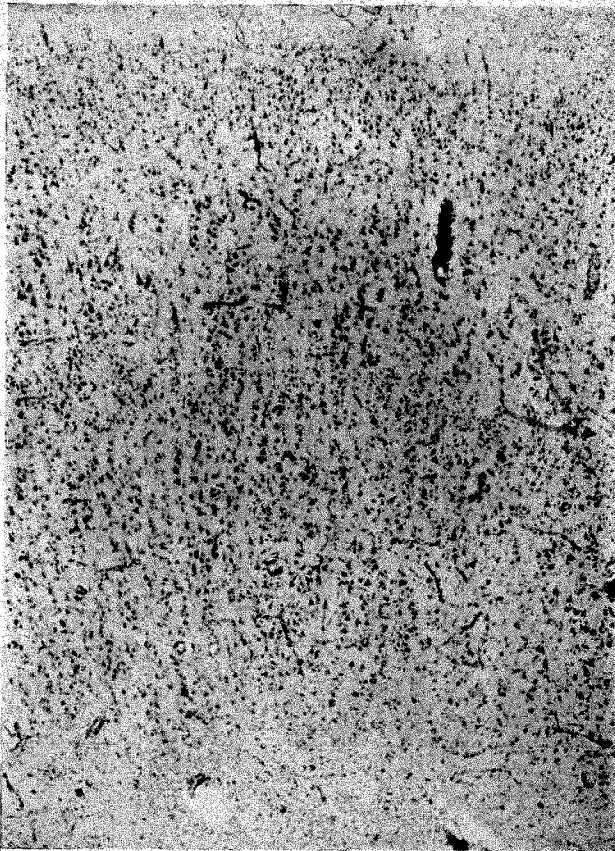


FIG. 6.—Nissl stain. Granular frontal area ; six weeks after treatment. A case showing the least accumulation of infiltration on the small blood-vessels. This and fig. 5 represent thus two extremes, the other case falls in between.

Group III.—THREE CASES, DYING THREE TO SIX WEEKS AFTER TREATMENT.

• *Clinical.*—One patient, without showing improvement, developed a bronchitis and cyanosis, increasing until death. The second had hallucinations, was excited, then gradually became weaker, developed a phlegmon and died in a

state of marasmus. The third became somewhat maniacal and excited, gradually grew weaker and died of circulatory failure. All cases had six to ten elevations of temperature.

Histological.—In this period the severity of the histological changes reaches its maximum, but after this stage gradually diminishes.

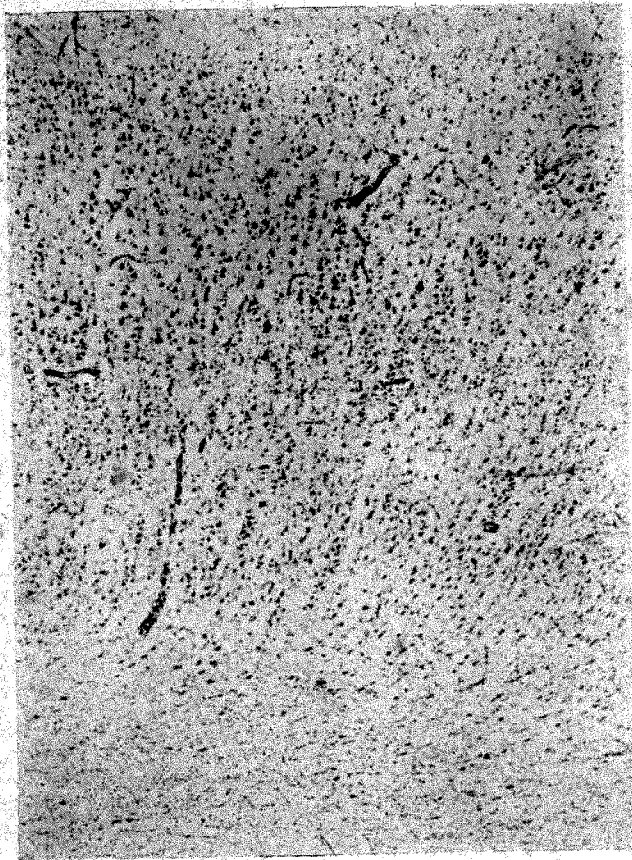


FIG. 7.—Nissl stain. Granular frontal area; three months after treatment. The diminution of infiltration and the improved appearance of the cortical architecture are evident.

The intensity of the meningeal infiltration is essentially the same, but has undergone a change in character, in that the plasma cells are now quite as numerous as the lymphocytes. The macrophages are considerably reduced. The perivascular infiltration in the cortex is even greater, but its character has changed in that the capillaries are somewhat less strongly infiltrated, while thicker accumulations on the arterioles and the venules tend to characterize the picture (figs. 5 and 6). The infiltration is becoming less diffuse than in the cases dying during treatment.

The macroglia, especially strongly proliferated between four to fourteen days after treatment, is now even less proliferated than during treatment, while the microglia at this time is enormously increased. Of all periods none gives such a strong iron reaction or shows such a proliferation of microglia.

The cortical architecture is perhaps somewhat less disturbed than in the earlier cases. No spirochaetes were found.

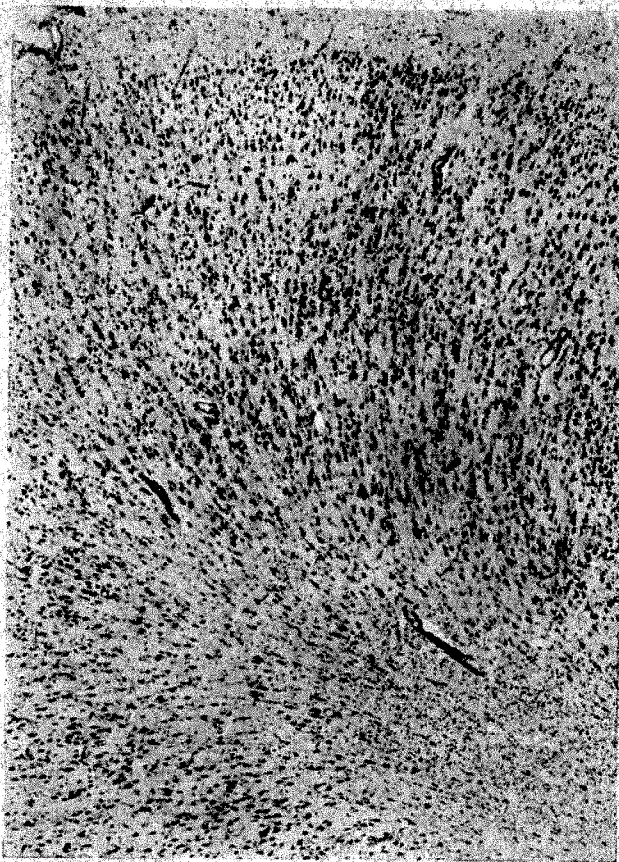


FIG. 8.—Nissl stain. Granular frontal area; nine months after treatment. The cortex shows continued restoration.

Group IV.—FIVE CASES, DYING THREE TO FIVE MONTHS AFTER TREATMENT.

• *Clinical.*—Three of these cases became steadily worse, both physically and mentally; one terminated in pneumonia, the other two were excited, one dying suddenly in a bath, the other as a result of a broken rib. All cases had six to eleven elevations of temperature.

Histological.—In this period one sees fairly marked regression of practically all changes. The infiltration of the meninges is much less; particularly marked is the decrease of plasma cells. The cortical perivascular infiltration has become considerably reduced, especially around the capillaries. It is confined chiefly to the arterioles and venules, which show here and there small accumulations of lymphocytes and plasma cells in the adventitial spaces.



FIG. 9.—Nissl stain. Intermedial frontal area; six months after treatment. Inflammatory focus of massively infiltrated vessels, the cells breaking through into the nervous substance. In this case spirochaetes were found.

The proliferation of the glia has become considerably less. The most striking improvements of all are the diminution in the iron content of the blood-vessels and microglia, the decrease in the proliferation of the microglia and the reduction of plasma cells in the meninges. The architecture of the cortex now, for the first time, has a more normal appearance.

Fig. 7 represents the average appearance of this group, and in comparing

it with the previous micrographs one is able to recognize a diminution of infiltration and a more orderly arrangement of the nerve-cells. No spirochaetes were found.

Group V.—FOUR CASES, DYING SIX TO NINE MONTHS AFTER TREATMENT.

Clinical.—These cases all presented very much the same clinical course: gradual physical and mental deterioration without improvement; restlessness or severe excited states; one patient died in such a state after having had hallucinations earlier. The cases had nine to ten rises of temperature.

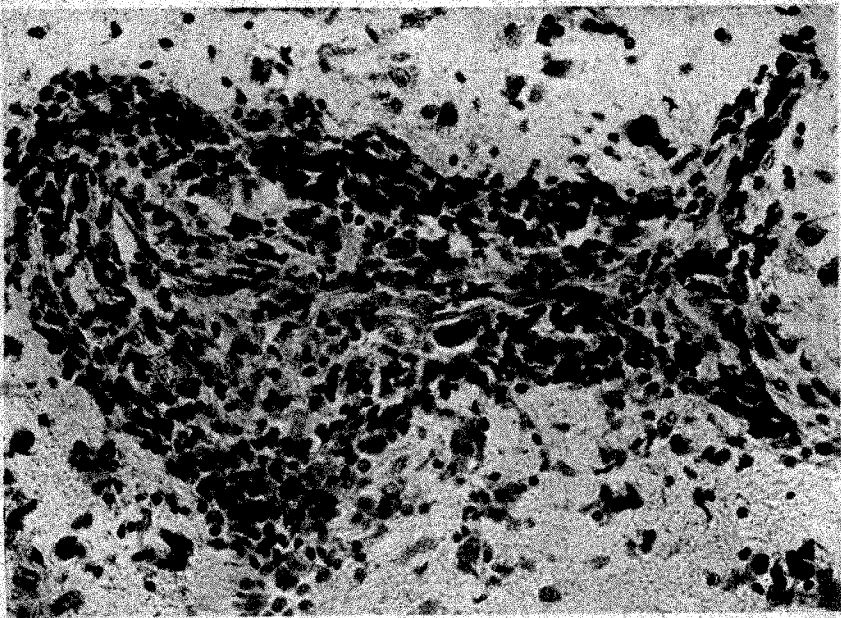


FIG. 10.—Nissl stain. Same case as fig. 9. The vessel is represented by a dense strongly infiltrated mesenchymatous mesh with obliteration of the lumen. (Unorganized granuloma, Jakob.)

Histological.—At this time a second point of significance is reached. Either the improvement continues still further, or a severe and rather unusual inflammatory reaction is to be seen. In three cases there is a still further regression of practically all histological changes. The infiltration has diminished further, but remains predominantly plasma cell in type. The iron content of the walls of the blood-vessels and of the microglia has undergone further reduction. There is still less proliferation of the microglia. The cortical architecture, too, shows considerable improvement (fig. 8). In these three cases I was unable to find any spirochaetes.

In the fourth case the changes are more severe than in any of the previously described twenty-four cases, and differ also in character. In the former cases the infiltration was fairly uniform; here it is most irregular in intensity in different areas (*herdförmig*). Whereas in most regions of the cortex one finds only a few plasma cells and lymphocytes along the capillaries and numerous small vessels with rings of infiltration consisting chiefly of lymphocytes there are numerous areas of intense infiltration in which there is marked proliferation of the walls of the larger vessels, which often has led to considerable narrowing of the lumen, and in this mesenchymal network are embedded many infiltrating cells, some of which are plasma cells, but most lymphocytes. The infiltration no longer remains within the confines of the *membrana limitans* but has broken through into the nervous tissue itself (figs. 9 and 10). The capillaries and smaller vessels are most severely infiltrated and numerous lymphocytes are scattered throughout the adjacent nervous tissue. Rod cells are extremely abundant in these areas and are more numerous than in any of the cases thus far considered. The macroglia cells, too, are present in great numbers and there is a considerable increase of their protoplasm so that the cell bodies appear round and swollen. The blood-vessel walls and microglia give an unusually strong iron reaction. Fig. 9 shows clearly the severe disturbance in the architecture of the cortex. In this case spirochætes were found.

I wish to emphasize the fact that, after the beginning of restitution, spirochætes were not found in any case until six months after treatment. In the above case, the first in which they were found after this interval, the histological changes are of a very different character from any found in the previously described cases (twenty-four), but resemble closely the changes found in the relapsing cases of the following group.

(Group VI.—TEN CASES, DYING ONE TO TWO-AND-A-HALF YEARS
AFTER TREATMENT.

Because of the clinical as well as the histological complexity of this group, it seems advisable to give a short summary of the clinical course of each case, and for the sake of better comparison I shall consider first those with insignificant histological findings, then the cases with severe changes.

(A) *Five Cases with Slight Histological Changes.*

Case 26 (Sau.).—Admitted May 14, 1924. The patient was excited, euphoric and expansive. Blood Wassermann +++; C.S.F. Wassermann 3-4-4; cells, 111, N.A. +; Wb. + + +, mastic, very strong paretic curve.

¹ C.S.F. Wassermann = 3-4-4 according to amount of C.S.F. used, i.e., 0.2-0.5-1.0 N.A. = Nonne-Apelt test for globulin. Wb. = Weichbrodt's reaction for globulin. Mastic (normomastic technique) is indicated as very strong paretic curve (7-9-12-12-12-12-11-9-6 5-5-4-4-3), strong, weak, very weak, lues cerebri or typical lues cerebri curve (3-4-6-8-7-6-5-4 4-3-3-3-2-2).

June 10, 1924: Inoculated with tertian malaria, ten rises of temperature.

July 8, 1924: Blood Wassermann + + + +; C.S.F. Wassermann 4-4-4; cells, 4; N.A. +; Wb. +, mastic: strong paretic curve.

August 26, 1924: The patient was quieter and mentally clearer. Blood Wassermann + + + +; C.S.F. Wassermann 1-4-4; cells, 6; N.A. +; mastic: lues cerebri curve.

January, 1925: Further mental deterioration became evident, associated with hallucinations. Later the deterioration became more rapid, the patient became dyspnoic, increasingly oedematous, finally stuporous, and died July 22, 1925.

Case 27 (Mut.).—Admitted January 10, 1923. The patient was expansive, and exhibited considerable defect of memory and speech. Blood Wassermann + + + +; C.S.F. Wassermann 3-3-3; cells, 92; N.A. + +; Wb. + + +.

January 31, 1923: C.S.F. Wassermann 3-3-3; cells, 28; N.A. + +; Wb. + + +.

February 3, 1923: Inoculated with tertian malaria; seven rises of temperature.

March 2, 1923: The patient was little changed, continuing euphoric, expansive and profane. Blood Wassermann + + + +; C.S.F. Wassermann 3-3-3; cells, 21; N.A. + +; Wb., slightly opalescent.

April 5, 1923: Blood Wassermann + + + +; C.S.F. Wassermann 1-3-3; cells, 14; N.A. opalescent; Wb. $\pm$.

May 5, 1923: Blood Wassermann + + + +; C.S.F. Wassermann 3-3-3; cells, 14; N.A. opalescent; Wb. $\pm$.

June, 1923: The patient showed some improvement, though he continued expansive.

July, 1923: Improvement was such that the patient, no longer expressing expansive ideas, was able to play cards. Blood Wassermann + + + +; C.S.F. Wassermann 3-3-3; cells, 9; N.A. $\pm$; Wb. +.

September, 1923: Tube feeding became necessary and deterioration continued. Died January 16, 1924.

Case 28 (Fan.).—Admitted July 28, 1923. The patient was confused, had hallucinations, and exhibited defects in speech and in writing. Blood Wassermann + + + +; C.S.F. Wassermann 3-3-3; cells, 77; N.A. opalescent, Wb. + +.

August 1, 1923: Inoculated with tertian malaria. fourteen rises of temperature.

September 10, 1923: He was manifesting increasing dementia and had several convulsive attacks. Blood Wassermann + + + +; C.S.F. Wassermann 0-2-3; cells, 4; N.A. $\pm$; Wb. + +; mastic: strong paretic curve.

October 2, 1923: No improvement. Blood Wassermann + + + +; C.S.F. Wassermann 1-3-3; cells, 5; mastic: very weak paretic curve.

January, 1924: The patient developed progressive dementia. Blood Wassermann + + + +; C.S.F. Wassermann 2-3-3; cells, 2; N.A. opalescent, Wb. +; mastic strong paretic curve. Continuing downhill the patient became emaciated and developed decubitus. Died November 20, 1924.

Case 29 (Ref.).—Admitted September 22, 1923. The patient was at times depressed, at times expansive. Blood Wassermann negative (Stern +++); C.S.F. Wassermann 1-1-3; cells 15; N.A. opalescent; Wb. +.

October 2, 1923: Inoculated with tropical malaria; four rises of temperature.

November 15, 1923: No improvement. Blood Wassermann negative; C.S.F. Wassermann 0-1-3; cells 4; N.A. trace opalescence; Wb., opalescent; mastic: strong paretic curve.

1924: His condition became slowly worse and there were occasional convulsive attacks.

January, 1925: Blood Wassermann negative (Stern ++); C.S.F. Wassermann 1-3-3; cells 18; N.A. ±; mastic: very weak paretic curve. The patient became increasingly indifferent and demented until death from heart failure, April 15, 1925.

Case 30 (Hed.).—Admitted October 30, 1922. The patient was confused and showed considerable mental deterioration. C.S.F. Wassermann 2-3-3; mastic: strong paretic curve.

November 11, 1922: Inoculated with tertian malaria; seven rises of temperature.

January 23, 1923: The patient had been able to work fairly well about the hospital and had improved sufficiently to be discharged.

February 18, 1924: Re-admitted because of an attack of unconsciousness a few days before. He had previously been well. Blood Wassermann negative; C.S.F. Wassermann 0-2-3; cells 3; N.A. trace of opalescence; Wb. opalescent; mastic: very weak paretic curve. He was depressed and indifferent, but improved rapidly and was discharged again March 31, 1924.

November 15, 1924: Re-admitted because of depression and an attempt at suicide. He was restless and noisy. His anaemia, marked on admission, became steadily worse. Death, November 24, 1924.

(B) FIVE CASES WITH SEVERE HISTOLOGICAL CHANGES.

Case 31 (Rud.).—On admission, November 20, 1924, the patient was euphoric and indifferent. Blood Wassermann + + + +; C.S.F. Wassermann 0-1-3; cells 22; N.A. opalescent; Wb. +; mastic: very strong paretic curve.

December 3, 1924: Inoculated with tertian malaria; seven rises of temperature.

April, 1925: The patient had become gradually worse, continuing euphoric and wholly without insight. Blood Wassermann + + + +; C.S.F. Wassermann 0-0-2; cells 69; N.A. +; mastic: strong paretic curve.

September, 1925: Blood Wassermann + + + +; C.S.F. Wassermann 4-4-4; cells 64; mastic: very strong paretic curve. There was gradual deterioration until death by suffocation while eating, November 13, 1925.

Case 32 (Jac.).—On admission, June 14, 1924, the patient was considerably demented, indifferent, and profane. Blood Wassermann + + +; C.S.F. Wassermann 2-4-4; mastic: weak paretic curve.

July 10, 1924. Inoculated with tertian malaria; seven rises of temperature. November, 1924: No improvement. Blood Wassermann ++++; C.S.F. Wassermann 2-4-4, cells 10; N.A. trace opalescence; Wb. opalescent; mastic: weak paretic curve.

February, 1925. The patient had hallucinations, was confused and indifferent.

March, 1925. He was euphoric and indifferent. He became gradually emaciated. Died, April 11, 1926.

Case 33 (Rat.).—On admission, January 15, 1923, the patient was markedly demented and showed defects in speech and writing. Blood Wassermann ++++; C.S.F. Wassermann 3-3-3; cells 260; N.A. +; Wb. ++.

February 1, 1923. Inoculated with tertian malaria. Nine rises of temperature.

March 1, 1923: Blood Wassermann ++++, C.S.F. Wassermann 3-3-3, cells 15; N.A. ++; Wb. ++.

July, 1923: Blood Wassermann ++ (Stern +); C.S.F. Wassermann 3-3-3, cells 5; N.A. ±, Wb. ++. The patient had improved and was discharged in a fairly good remission.

February, 1924. Re-admitted, more confused and indifferent. Blood Wassermann ++++; C.S.F. Wassermann 4-4-4; cells 11; N.A. +; Wb. ++; mastic: strong paretic curve. After improving slightly for a time he showed more rapid mental deterioration, and towards the end developed decubitus. He died November 23, 1925.

Case 34 (Rev.).—On admission, September 7, 1923, the patient was confused, indifferent, demented, and at times excited. Within the first few days he had three convulsive attacks. Blood Wassermann ++++; C.S.F. Wassermann 3-3-3; cells 516; N.A. +.

October 6, 1923: Inoculated with tertian malaria, and had typical rises of temperature—number unknown.

January 9, 1924: The patient showed no improvement, was very noisy, euphoric and restless. He was without insight and developed progressive dementia. Blood Wassermann ++++; C.S.F. Wassermann 3-3-3; mastic: lues cerebri curve.

April, 1924: He had improved enough to work about the hospital, and to be discharged in August, 1924.

July, 1925. Re-admitted because of sudden loss of speech. He was indifferent and showed increased dementia. Blood Wassermann ++++; C.S.F. Wassermann 4-4-4; cells 390; N.A. ±; mastic: very strong paretic curve.

October, 1925. The patient continued downhill and had several convulsive attacks.

February, 1926: He was becoming progressively demented, very restless and noisy, and later increasingly emaciated until he died May, 1926.

Case 35 (Kei).—On admission June 23, 1923, the patient was confused and very irascible. Blood Wassermann ++++, C.S.F. Wassermann 3-3-3; cells 11; mastic: strong paretic curve.

July 2, 1923 : Inoculated with tertian malaria ; eight rises of temperature.

August 24, 1923 : Considerable improvement. C.S.F. Wassermann 3-3-3 ; cells 16 ; N.A. negative ; Wb. + ; mastic : typical lues cerebri curve.

November 23, 1923 : She was discharged in a fairly good remission and was able to carry on housework and conduct a store.

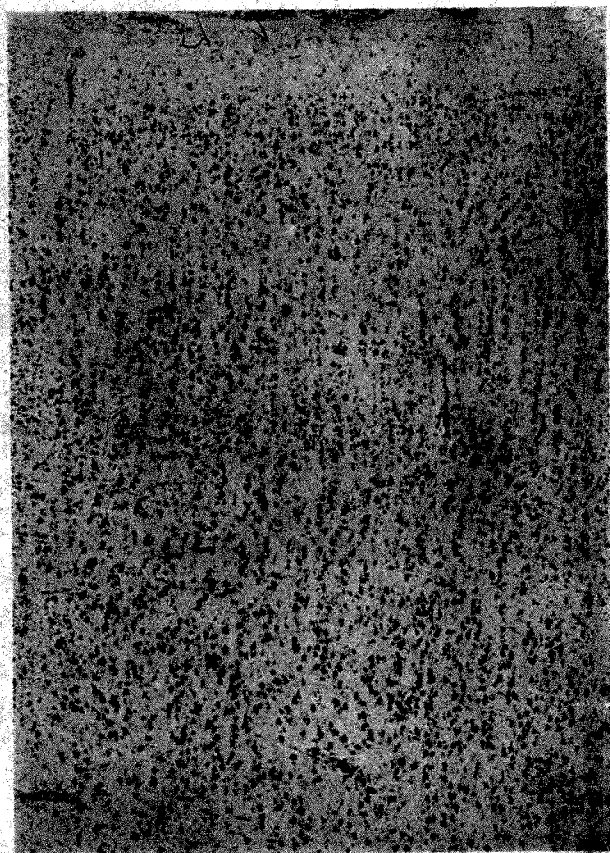


FIG. 11.—Case Sau. Nissl stain. Superior parietal area; one year after treatment. Except for evident loss of ganglion cells the cortex presents a fairly good appearance.

July, 1924 : Re-admitted. She was confused, irascible and without insight. C.S.F. Wassermann 3-3-3 ; cells 90 ; N.A. +. She became progressively demented and had a convulsive seizure on the day before death, October 10, 1924.

Histological.—The first five cases (Group A) present very much the same histological picture as the three cases of the preceding group (six to nine months). The changes are slight ; the meningeal infiltration is of only a mild degree, but there is a fairly marked relative increase of macrophages.

Of interest is the further improvement in the appearance of the cortical architecture (fig. 11). A fairly marked loss of ganglion cells is obvious at once (numerous small areas devoid of cells are evident in the photomicrographs), which clearly indicates that considerable destruction has already been effected. Nor can one speak of normal ganglion cells, for there is a great variety of changes to be seen in them. Nevertheless the orderliness of the nerve cells and the much neater arrangement of their layers, as compared with those cases terminating early after treatment and with the usual cases of general paralysis, is at least impressive. This in itself does not speak for a very active destructive or degenerative process.

The infiltration of the cortical blood-vessels is also very slight, only a few lymphocytes and plasma cells being found here and there on the smaller vessels, more rarely still on the capillaries.

It is surprising, in view of these findings, that the microglia is more strongly proliferated than in the preceding period. The iron reaction in the blood-vessels and microglia has become stronger.

In none of these cases was I able to find spirochaetes.

In striking contrast to the findings in the first five cases are those of the following five of the same period, one to two-and-a-half years after treatment (Group B). The latter present very much the same reaction as the case (Tim) of six to nine months (fig. 10) and also show some tendency towards a more focal distribution of inflammation, with variations of the picture in different cases. For example, in the case (Rev.) there are only a few lymphocytes and plasma cells along the capillaries and in some areas occasional, in other areas many, larger vessels with thick infiltration rings, in most of which plasma cells predominate, though in some lymphocytes are in the majority. In the case (Rat.) the capillaries are as a rule rather strongly infiltrated with plasma cells, but in some places the perivascular infiltration forms thick rings in which occasionally the cells show a tendency to be arranged in layers. In the other three cases the capillaries show from a very slight to a moderate degree of infiltration; the small vessels, in some areas, present all degrees of mesenchymal proliferation, with increasing organization of the infiltrating elements to the formation of miliary gummata, as in case (Rud.) (figs. 12 and 14). The iron reaction in these cases is very marked, in fact greater than in any group of cases except those dying in three to six weeks. There is the same moderate degree of proliferation of the microglia and the macroglia as in the preceding five cases. The disturbance of the cortical parenchyma is of a moderate severity, and is more pronounced where the inflammatory foci are situated. Whereas in the first five cases of this period with only slight changes no spirochaetes were found, spirochaetes were found in four of the last five.

Group VII.—THREE CASES, THREE TO FIVE YEARS AFTER TREATMENT.

These three cases present rather varied histological pictures, and so it seems advisable to give briefly the more outstanding features of each case.



FIG. 12.—Case Rud. Nissl stain. Eleven months after treatment. Inflammatory focus. In the thickened walls of the larger vessel the infiltration is organized in layers.

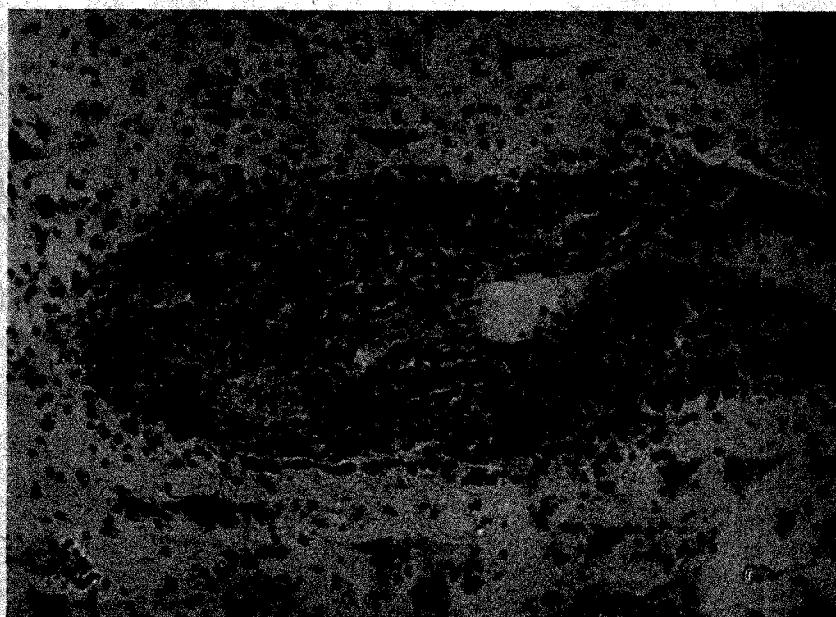


FIG. 13.—Nissl stain. Same case as fig. 12. The massively infiltrated mesenchymal mass forms a considerable excrescence in the vessel wall. In the centre areas of paleness are evident.

Case 36 (Wie.).—Admitted September 6, 1921, with marked euphoria and considerable speech defect. Blood Wassermann +++ ; C.S.F. Wassermann 3-3-3; cells 15; N.A. +; Wb. +; mastic: weak paretic curve.

September 12, 1921: Inoculated with tertian malaria; eleven rises of temperature.

November 4, 1921: He was quiet, able to help with the work, possessed insight into his condition and could be discharged November 21, 1921. At home he continued to improve.

July, 1922: Readmitted because of convulsive attacks. He was at times apathetic, at times euphoric. C.S.F. Wassermann 3-3-3.



FIG. 14.—Nissl stain. Same case as fig. 12. Miliary gumma with necrosis and giant cells.

October, 1922: No improvement. He had several convulsive attacks.

1923-24: Dementia gradually increased, associated with occasional convulsive attacks. March, 1924: Blood Wassermann ±; C.S.F. Wassermann 3-3-3; cells 34; N.A. +; mastic: very strong paretic curve.

January, 1925: He was almost totally demented, and he died on February 2, 1925.

• *Histological.*—The meninges are only slightly thickened. The infiltration is of a very mild degree, lymphocytes and plasma cells being equally numerous. Quite a number of mast cells are scattered throughout. The several cortical layers present very little disorder, though many ganglion cells have fallen out.

The cortical perivascular infiltration is that of a mild paretic type, with some proliferation of the microglia and a feeble iron reaction in the walls of the blood-vessels and in the microglia.

Case 37 (Bec. W.).—On admission, October 12, 1920, the patient was disoriented, demented and euphoric.

October 21, 1920: Inoculated with tertian malaria; two rises of temperature.

1921-23: Slowly increasing dementia, with occasional convulsive attacks.

September, 1924: Re-inoculated with tertian malaria, but no typical rises of temperature followed, though he ran a slightly febrile course for six days. Afterwards dementia became steadily more marked and he became more and more emaciated. He died in October, 1925.

Histological.—The parenchymatous changes as well as intensity of the inflammatory reactions are somewhat more severe than in the previous case. In three areas there is intense perivascular infiltration, with numerous cells breaking into the brain substance, and in two of these areas mesenchymal proliferation is marked. The iron reaction in this case is of a slight degree, the microglial proliferation fairly pronounced. Numerous mast cells are found in the meninges, fewer in the cortical perivascular spaces. No spirochaetes were found.

Case 38 (Wul.).—On admission, October 10, 1922, the patient was demented and had disturbances of speech. Blood Wassermann +++; C.S.F. Wassermann 3-3-3; cells 286; N.A. $\pm$; Wb. ++.

October 20, 1922: Inoculated with tertian malaria; seven rises of temperature.

November, 1922: C.S.F. Wassermann 3-3-3; cells 41; N.A. $\pm$; Wb. +; mastic: very strong paretic curve.

December, 1922: C.S.F. Wassermann 3-3-3; cells 35; N.A. +; Wb. ++.

January, 1923: Blood Wassermann +++; C.S.F. Wassermann 3-3-3; cells 17; N.A. $\pm$.

February, 1923: The patient had improved enough to help in the ward, but was euphoric. Blood Wassermann +++; C.S.F. Wassermann 3-3-3; cells 11; N.A. opalescent; mastic: strong paretic curve.

March, 1923: Blood Wassermann ++; C.S.F. Wassermann 3-3-3; cells 14; N.A. $\pm$.

April, 1923: Blood Wassermann +++; C.S.F. Wassermann 2-3-3; cells 31; N.A. $\pm$; Wb. ++; mastic: weak paretic curve.

February, 1924: The patient continued to help with the ward work, though his condition remained practically the same as the year before. Blood Wassermann, $\pm$; C.F.S. Wassermann 3-3-3; cells, 25; N.A. opalescent; mastic: weak paretic curve.

June, 1924: The patient was working regularly in the garden, reading, playing cards, and quite orderly in his habits, though he continued slightly euphoric. Blood Wassermann ++++; C.S.F. Wassermann 1-3-4; cells, 8; N.A. $\pm$; Wb. $\pm$; mastic: weak paretic curve.

May, 1925: The patient was no longer capable of working in the garden. He remained in bed quite indifferent and filthy in his habits. He died September, 1926.

Histological.—The meninges show a moderate degree of thickening and of inflammation. In the cortex there is marked architectural disturbance, and a considerable loss of ganglion cells. The perivascular infiltration is in all pre-

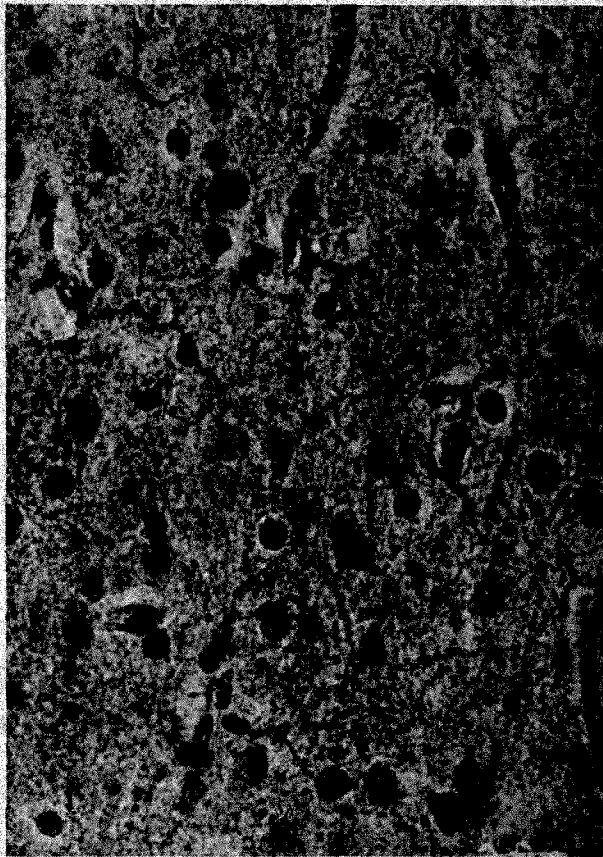


FIG. 15.—Case Mey. Hortega silver method. An area in which the microglia was found most strongly proliferated.

parations noticeable, and in many areas very pronounced. Many vessels have thickened walls, some so thickened as to obliterate almost completely the lumen. The thickened walls are a spongy mesenchymal net, the meshes of which are filled with infiltrating cells which frequently break into the nervous tissue. These correspond to the "unorganized granuloma" of Jakob. Occasionally pale areas are encountered in the centre of such a granu-

loma, and rarely a giant cell may be found adjoining it. This, no doubt, represents an early miliary gumma. The microglia is considerably proliferated and swollen macroglia cells are very numerous. There is an unusually strong iron reaction in the walls of the blood-vessels and in the microglia cells; the oligodendroglia and macroglia also contain a noticeable amount of iron. Spirochaetes were found. This case thus corresponds rather closely to the

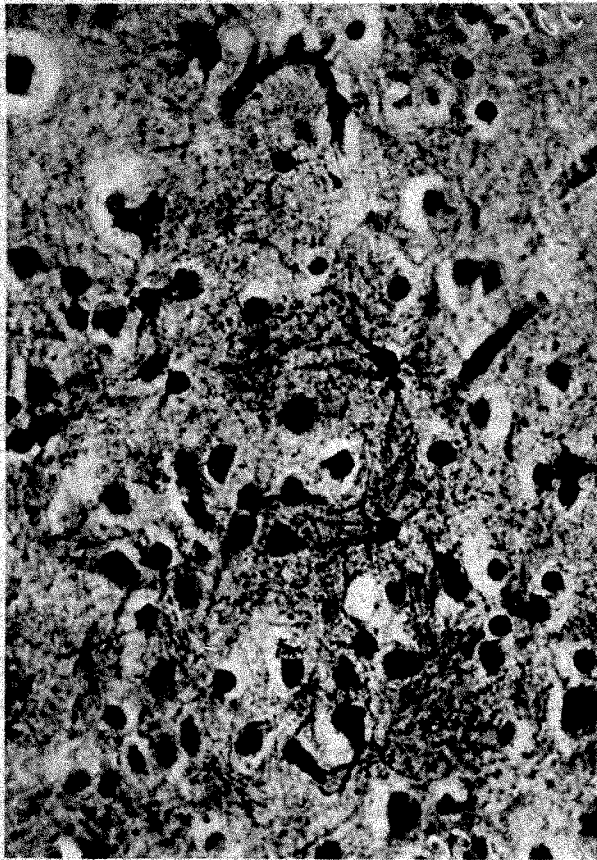


FIG. 16.—*Case Mey.* Cajal's gold chloride method. Condition where the macroglia was found most markedly proliferated.

five cases of the one to two-and-a-half years period, that showed such marked histological changes, and in 80 per cent. of which spirochaetes were found.

The other two cases, in which there were far less marked changes, cannot be identified with any of the previously described groups. Both show typical parietic changes, the first of a very mild degree as judged by the severity of parenchymatous changes, the intensity of infiltration, the glial proliferation

and the iron reaction, while the second is of greater severity. Nevertheless, these two cases, in contrast with the above case in which spirochaetes were found, resemble more closely those of the period one to two and a half years, in which no spirochaetes could be discovered, and in which the histological changes were slight.

In connection with these cases, which were clinically and histologically general paresis, it may be of interest to consider the findings in a case dying during a remission.

Case 39 (Mey).—(Observed and treated by Professor Jakob.)

Clinical.—Female, aged 43, May 3, 1923. She had no knowledge of luetic infection. For one year there had been mental change, especially poor memory, sleeplessness, impaired judgment, periods of depression, negligence of household, intellectual deterioration and speech disturbance. Her pupils were irregular and reacted poorly to light. Blood Wassermann +++ ; C.S.F. Wassermann ++++ ; mastic: general paralytic curve.

May 8, 1923: Inoculated with malaria; first rise of temperature three days later; in all eight rises. Directly after the treatment the patient showed improvement, which continued until she was able to resume her social life and discharge fully her household duties. Death occurred in October, 1926, following operation for carcinoma of the stomach.

Histological.—The meninges are thickened to a moderate degree and slightly infiltrated, chiefly with lymphocytes, in fact in many areas plasma cells are extremely rare. The cortex shows little disturbance. The ganglion cells and the different layers present a very orderly arrangement. Numerous small areas devoid of ganglion cells suggest, however, that considerable destruction has already taken place. Here and there are arterioles with thickened fibrous walls. In some sections a few plasma cells and lymphocytes are encountered in the perivascular spaces, but in most they are rare. The microglia and macroglia are practically normal. Figs. 15 and 16 were taken from areas where they were richest in protoplasmic processes. The iron reaction in the walls of the blood-vessels is moderately strong, and a considerable amount of iron is found in the macroglia but much less in the oligodendroglia. Practically no iron could be found in the microglia. No spirochaetes were seen. This case shows clearly how far restitution may go.

Having pointed out the more striking histological change at various intervals after treatment by malaria, I can now review my findings, in conjunction with those of other investigators, in an effort to present a picture of the series of histological reactions most likely to occur in the brain following inoculation with the malarial parasite.

* In order to facilitate comparison, I have attempted in each block of tissue to estimate the intensity of the various reactions, and have designated this as +, ++, +++, and ++++. On this basis, it was possible to construct a chart showing the severity of the changes during

treatment and at different periods after the treatment (fig. 17). In this chart I have not included the six cases in which there was a recrudescence of inflammation, since this differed in character to such a

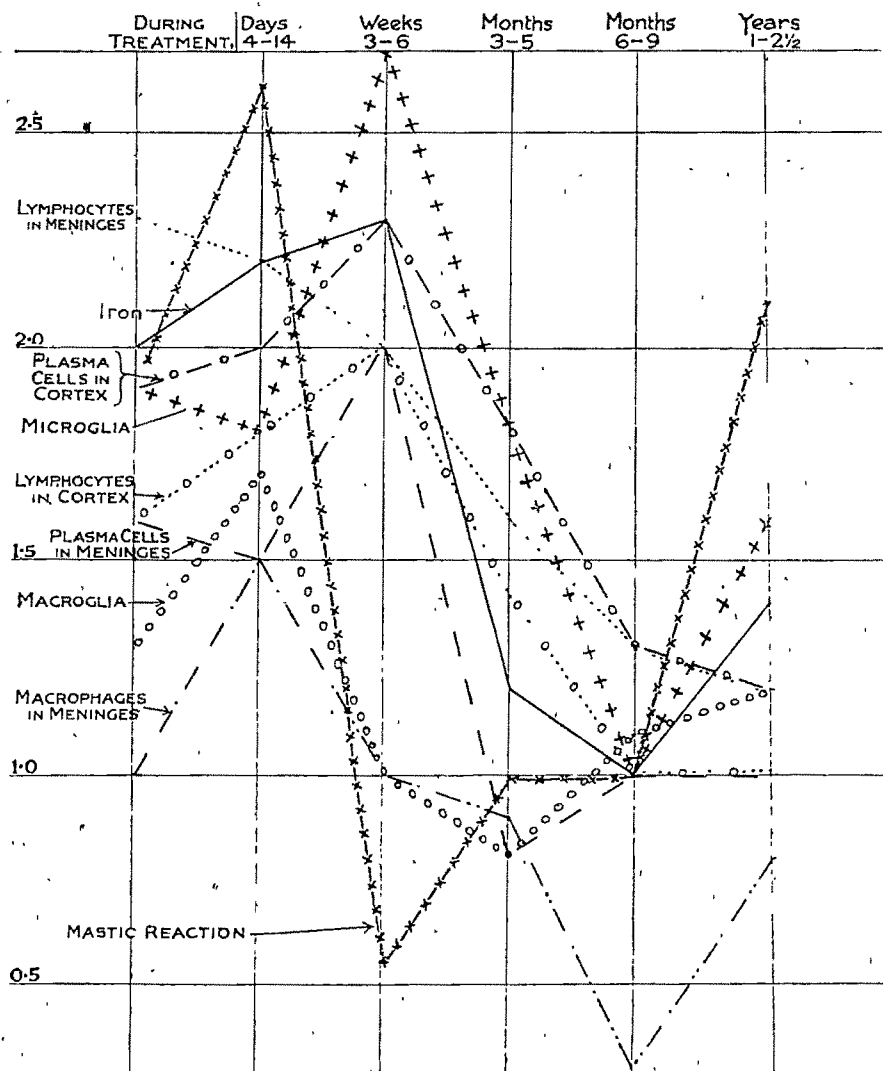


FIG. 17.—Chart indicating the intensity of the various reactions at successive intervals after treatment.

degree that the intensity could not be estimated by the same standards employed for the other cases.

Roughly, three divisions become at once possible. *First, a period*

of *exacerbation* of all changes, commencing during treatment and persisting until from three to six weeks after treatment. *Second*, following the period of exacerbation, a *period of restoration*, which may continue uninterrupted for years (in about half of my cases). *Third* (in the other half of my cases), there may take place, any time after six months, a new flare up in the histological process, a *period of recrudescence*.

PERIOD OF EXACERBATION (SIXTEEN CASES).

During treatment and up to three to six weeks after treatment, the typical picture of general paralysis in its severest form is found. This includes derangement of the cortical layers and of the nerve-cells; meningeal and cortical perivascular infiltration; macroglial and microglial proliferation, and a strong iron reaction in the walls of the blood-vessel and in the microglia.

The lymphocytes in the meninges are most numerous during treatment, and diminish gradually thereafter. Other infiltrative reactions as well as glial proliferation, although pronounced during treatment, become even more intense shortly after the end of treatment. Most reactions increase gradually and reach their maximum between three to six weeks. Only the macrophages in the meninges and the macroglia form exceptions to this, exhibiting the strongest reaction from four to fourteen days after treatment, and then gradually diminish. The diffuseness of the infiltration, so characteristic of cases dying during treatment, becomes gradually less marked towards the end of this period. That is to say, whereas during treatment the infiltration is very intense on all vessels, later the capillary infiltration becomes less, and one finds thicker rings of infiltration on the arterioles and venules.

This increase in the intensity of inflammation is in accord with most previous studies. Kirschbaum [20] reports considerable variation in the intensity of the changes in his twenty-two cases. Nevertheless, the cases showing the severest changes were those dying within the first two weeks, those terminating fatally after one month presented rather slight changes. Only Lehoczky [23] found a diminution of the inflammatory reaction immediately following treatment, but his observations, based on five cases, are hardly convincing in view of contrary findings in 137 cases by various investigators, including forty-seven of my own.

It has been suggested by some, as Sträussler and Koskinas [37], that a change in the character of the histological picture also takes place immediately after malarial treatment, that the "malignant"

paralytic process is at least in part replaced by the "benign" more specific granuloma. As nearly as I can determine this conclusion is based on the finding of military gummata in two of their thirty-eight cases. However, since in their original description of these cases [36] they do not mention such findings, it may be assumed that they were not very prominent. Kirschbaum [20] reports finding military gummata in two cases out of twenty-two, one of which died shortly after treatment, but he was inclined to view this as merely incidental, and not as indicative of a real qualitative change in the process. Freeman [5], though reporting no military gummata, does emphasize the organization of the exudate soon after treatment, in the meninges as well as in the cortical perivascular spaces. The evidence in favour of the view that malaria causes an immediate change to a more specific reaction is slight. That such changes may occasionally be found in general paralysis untreated with malaria was pointed out by Strüssler himself in 1906 [34], and in 1910 [35], and also by Jakob [15]. There is no obvious reason why they may not also occasionally occur in cases treated with malaria, without indicating any causal relationship.

The appearance of gummata in other parts of the body following malarial treatment is very striking. Markusiewicz [25] reported in 1925 a case of typical general paralysis that had had a luetic infection twenty years before. The patient was inoculated with malaria, had nine rises of temperature, and about two months afterwards typical gummata appeared on the forehead and chest. The diagnosis was confirmed histologically. The same year Schulze [30] described three cases that developed typical tertiary syphilitic skin lesions in the first month after treatment. In 1926 Pfeiffer [28] reported a case of general paralysis which had been inoculated with malaria and had twelve elevations of temperature. About six weeks later three hard nodules appeared on both sides with soft centres; they promptly disappeared after injection of salvarsan. In 1927 Kirschbaum [21] described a case of gumma in the throat one and a half years after malarial inoculation; it disappeared in a short time after the use of iodine and salvarsan. The same year Balaban [2] reported a similar case in which gummata developed during malarial treatment.

Interesting as these findings are, they are still too few to permit any definite conclusions. It is conceivable that they may be an indication of the profound influence of the malarial therapy on the entire organism, a disturbance of the usual relationship between the spirochaetes and the defence mechanism of the body. There is no conclusive evidence that

the malarial therapy may bring about such reactions in the central nervous system during or soon after treatment.

Several references have also been made to a predominance of lymphocytes. Sträussler and Koskinas, for example, state that lymphocytes characterize the picture, and not plasma cells: Nakamura found a preponderance of lymphocytes, and Freeman [5] says that "even as early as ten days after the onset of fever plasma cells are decidedly scarce" in the meninges. Others deny this, and my own cases do not show any such alteration in the relationship between lymphocytes and plasma cells. It is true that during treatment there was a predominantly lymphocytic infiltration of the meninges, but plasma cells were by no means scarce, and the cortical adventitial spaces showed the usual predominance of plasma cells.

The numerous macrophages found in the meninges during this period should, perhaps, be emphasized; this observation was made also by Sträussler and Koskinas in their first report. Their presence in such numbers would seem to indicate a rather active process, and is in keeping with the general exacerbation of all reactions.

The proliferation of the microglia is one of the most outstanding features of this period. Nakamura [27] found in his cases, two to sixteen days after treatment, an increase of glial nuclei, even the formation of clumps. He does not mention the type of glia, though, from his description, it is likely that he referred chiefly to macroglia. If so, his findings correspond to mine, as in these cases the greatest proliferation of macroglia occurred four to fourteen days after treatment.

In fig. 17 one is at once struck by the strong iron reaction at this stage, and its almost precipitous fall in the following period. In this chart only the iron in the blood-vessel walls is indicated but this may also be considered as representing the iron content of the microglia, since the two were found to run parallel; but the amount in the microglia is far less than that in the walls of the blood-vessels.

Spatz and Metz [31, 32] have pointed out this close relationship between the iron in the blood-vessel and that in the microglia, and are of the opinion that in paralysis the iron is of hæmatogenous origin, and that, as the result of an abnormal permeability of the inner layers of the blood-vessels, iron can easily be taken up from the blood-stream and transported into the tissues. They believe it highly improbable that the iron in general paralysis is the result of katabolic processes in the tissue. These authors also consider iron in the microglia peculiar to general paralysis. The findings in the forty-seven cases studied by me sub-

stantiate these observations. In only two cases did I find a moderately strong iron reaction in the oligodendroglia.

The state of the cerebrospinal fluid has led a number of investigators to the conclusion that an increase in the permeability of the blood-vessels does occur after malarial treatment. I shall return to this question in discussing the changes in the cerebro-spinal fluid.

PERIOD OF RESTITUTION.

After three to six weeks there is a steady improvement in the appearance of the cortex, and a gradual recession of infiltration, as well as a diminution of glial proliferation and of iron in the walls of the blood-vessels and microglia. The longer after treatment, the further has this restitution gone. The only exceptions to this are that between six and nine months there may be slight increase of plasma-cells in the meninges, and a slight increase in the proliferation of the macroglia.

In striking contrast to the general signs of improvement is the increase of macrophages in the meninges, the increased intensity of the microglial proliferation and of the iron reaction, found in the cases dying from one to two-and-a-half years after treatment. These reactions do not, however, reach the intensity of the period of exacerbation.

PERIOD OF RECRUDESCENCE.

It appears that after six months a new flare-up of inflammation may take place in certain cases. Furthermore, this new process differs considerably from the usually accepted picture of general paralysis. Among the four cases examined six to nine months after treatment, such a reaction occurred in one, and among the ten cases examined one to two-and-a-half years after treatment, in five.

Although the intensity of the process differs considerably in each case, the type of the reaction is so similar that the six cases may be considered together.

In each of them some degree of infiltration is found in practically all areas, but the characteristic feature is the small, scattered foci of severe inflammation. In such foci the walls of the blood-vessel are massively infiltrated, in most instances predominantly with lymphocytes, though occasionally there is found, in vessels with marked mesodermal proliferation, a predominance of plasma cells. The infiltrative elements break through the membrana limitans and come to lie free in the nervous tissue around the vessels, and often to such a degree that it is no longer possible to establish the boundaries of the vessel. Numerous blood-

vessels, in addition to the massive infiltration, show a strong mesodermal proliferation and some beginning organization. Here the infiltration tends to lie in layers embedded in this mesenchymal mesh (fig. 12). The lumen becomes narrowed, and may finally be completely obliterated (fig. 10). At times slight paleness is to be seen in the centre of this mesenchymal network, which probably indicates a beginning necrosis. Occasionally, the accumulation of infiltrative elements and mesodermal proliferation become so marked at some place in the vessel as to cause a protuberance on its wall (fig. 13). One sees thus the gradual increase of connective tissue elements from a beginning organization of the infiltration to the formation of a granuloma, with obliteration of the lumen of the blood-vessel and central pallor, and when this process goes still further miliary gummata with necrosis and giant cells develop.

There is a fairly strong iron reaction in the walls of the blood-vessels and in the microglia. Except in the one case examined six months after treatment, the microglia and macroglia are rather slightly proliferated.

Similar findings in cases of general paralysis were described in 1906 and in 1910 by Strüssler. He says [34] "that histologically the two processes develop alongside each other, whereby the luetic foci have served only as a stimulation to the increase in intensity of the paralytic process." In these cases there is no evidence of the paralytic process being exaggerated; on the contrary, the infiltration, except for these foci, is usually less intense.

In 1919, Jakob [15], in a series of fifty cases, described in considerable detail similar inflammatory foci. He dealt especially with cases showing acute exacerbations in association with general convulsive attacks ("Anfallsparalyse"). In such cases, he points out, this type of reaction is most often to be seen. He regarded the paralytic process as a malignant form of brain syphilis to which the defensive mechanism of the body failed to respond, and these inflammatory foci as a vigorous reaction against the invader, a tendency towards a more specific reaction, that is, towards *lues cerebri*, which is the benign form of cerebral syphilis. Spielmeyer [33], on the contrary, does not believe such inflammatory foci indicate a change in the type of reaction, but includes them in his conception of the histological picture of general paralysis. It is, therefore, merely a question of where the boundary between the two is to be established. Gummata certainly belong to the conception of *lues cerebri* rather than to general paralysis. As Jakob has pointed out, and as seen in my cases, all transition forms may be found, from the typical general

paralytic perivascular infiltration to gradual increase of mesenchymal tissue with obliteration of the lumen of the vessel, beginning paleness in the centre, later necrosis, and, finally, to the formation of miliary gummata with necrotic centres and giant cells. It seems obvious that these two forms of cerebral syphilis represent differences in the relationship between the defence mechanism of the body and the spirochæte. It is also conceivable that this relationship may, at some time in the course of the disease, be influenced by treatment, or, for that matter, by some general metabolic change. Such an alteration would naturally be expected to modify the histological picture. One would see then, not merely a general paralytic or a cerebral syphilitic process, but an indication of the manner in which the body has responded in defence against the invader.

In the six cases in which I have found evidence of recrudescence, at least it can be said that the process differs from that customarily found in general paralysis; and in its more focal distribution and predominance of mesodermal proliferation, even to the formation of miliary gummata, it tends more towards the type of reaction characteristic of *lues cerebri*.

It may be recalled that in the other cases, up to two years and a half after treatment, spirochætes were found only once (one case out of twenty-nine). It is well known how rarely spirochætes have been found in the brain after malarial treatment. My own findings are quite in keeping with this, and so one is almost forced to the conclusion that in most of the cases the spirochætes, if not entirely destroyed, are at least greatly reduced in number. It is true that Forster [4] has found them in two cases, in material removed by puncture during life. In the one case the material was removed seven weeks after treatment and so falls in the period of exacerbation; in the same period I found spirochætes in one case out of the first twenty-nine. It may be that at this stage, before the inflammation had subsided, the effects of the malarial therapy have not completed their destruction. In the second case reported by Forster the material was removed six months after treatment and so falls in the period where a recrudescence might be expected.

In striking contrast to the rarity of spirochætes in these twenty-nine cases is the fact that among the six cases which showed a focal distribution of the inflammation spirochætes were found in five. This can hardly be a coincidence. It would appear that this flare-up of focal inflammatory changes is related to the local presence of spirochætes.

When these results are reviewed it seems probable that as a result of the malaria treatment a tremendous destruction of spirochaetes takes place, and that if they are not completely destroyed they are, at least, rendered inactive for several months. In some cases where the spirochaetes have been incompletely destroyed, they may, after remaining dormant for about six months, regain their virulence, or proliferating, cause a recrudescence of inflammation. Not only is there a new flare-up, but there is a reaction unlike that of general paralysis, suggesting that the malarial therapy has in some way altered the distribution or the virulence of the spirochaetes and thus enabled the body to react differently, or that it has altered the reactive ability of the body itself.

In addition to the above more or less uncomplicated cases of general paresis, I have considered a group of six cases which developed, a shorter or longer time before death, convulsive attacks in which they died. These cases ("Anfallsparalyse"), according to some authors (Jakob, Jähnel), present rather characteristic changes, differing considerably from those usually found in general paralysis, and are to be regarded both clinically and histologically as a distinct group.

The following is a short summary of the clinical course and of the histological findings of these cases.

Case 40 (Rei).—(Treated in another hospital, number of rises of temperature unknown.) A maniacal, euphoric and demented patient, developed twelve days after the end of the treatment continuous convulsive attacks which ended in death three days later.

Histological.—With the exception of some endarteritic changes in the small cortical vessels, and small foci of softening in some areas, the usual picture of a moderately severe general paralytic is present.

Case 41 (Mag).—On admission, March 24, 1921, the patient was confused and expansive, and had marked disturbance of speech.

March 28, 1921: Inoculated with quartan malaria: eight rises of temperature.

May 5, 1921: The patient was little, if any, improved. C.S.F. Wassermann 0-1-3; cells 30; N.A. +.

September, 1921: Blood Wassermann +++; C.S.F. Wassermann 0-0-3 cells 16; N.A. ±; Wb. ++.

January, 1922: He had improved to the extent of being able to help in the ward.

February, 1924: Blood Wassermann +++; C.S.F. Wassermann 3-3-3; cells 19; N.A. ++; Wb. +++; mastic: weak parietic curve.

Re-inoculated with quartan malaria, five rises of temperature.

The condition became steadily worse, decubitis developed, he became markedly demented and had seven convulsive attacks, in the last of which he died, November, 1924.

Histological.—This case shows a most marked confusion of the layers of the cortex, and a very severe loss of ganglion cells. Perivascular infiltration, on the other hand, is slight, but is of the type and distribution usually found in general paralysis. Rod-shaped microglia cells are unusually numerous, and the macroglia is strongly proliferated. There is a considerable amount of iron in the walls of the blood-vessels and in the microglia. I was able to find spirochaetes in this case, but not in the other five of this group.

Case 42 (Kra.).—On admission, October 30, 1920, the patient was restless, euphoric and expansive. Blood Wassermann negative; C.S.F. Wassermann 3-3-3; cells 119.

November 12, 1920: Inoculated with tertian malaria; sixteen rises of temperature.

January 1921: The patient was much quieter. Blood Wassermann negative; (Stern +++); C.S.F. Wassermann 0-3-3, cells 10; N.A. +. He improved gradually and was discharged March, 1921.

April 29, 1922: Re-admitted: irascible and expansive.

May 2, 1922: *Re-inoculated with tertian malaria*, eight rises of temperature.

July, 1922: He had improved, and was able to work again about hospital, though was having occasional convulsive attacks. Blood Wassermann negative, C.S.F. Wassermann 3-3-3; cells 42; N.A. ±; Wb. ++.

September, 1922: C.S.F. Wassermann 3-3-3, cells 50; N.A. opalescent; Wb. +; mastic: strong paretic curve.

December, 1922. C.S.F. Wassermann 3-3-3; cells 50; N.A. ±; Wb. ++; mastic: very weak paretic curve.

January, 1923: The patient became gradually demented, and continued having occasional convulsive attacks until he died in status paralyticus, January, 1924.

Histological.—There is a fairly marked confusion of the cortical layers and loss of ganglion cells. The perivascular infiltration is considerable, predominantly plasma cells on the capillaries and smaller vessels, mostly lymphocytic mantles on the larger vessels, which often breaks through into the nervous tissue; an occasional vessel shows strong mesodermal proliferation. The microglia and macroglia are proliferated, though not strikingly so. The iron reaction in the blood-vessel walls and in the microglia is of moderate intensity.

Case 43 (Spr.).—On admission, April 4, 1923, the patient was without insight, excited and irascible. Blood Wassermann + + +.

April 30, 1923: Inoculated with tertian malaria, eight rises of temperature. During treatment, blood Wassermann ±; C.S.F. Wassermann 3-3-3; cells 48; N.A. ±; Wb. +.

June 1, 1923: Blood Wassermann negative (Stern ++), C.F.S. Wassermann 1-2-3; cells 5; N.A. +; Wb. ++; mastic: very strong paretic curve.

July, 1923: Blood Wassermann negative; C.S.F. Wassermann 1-2-3, cells 18; N.A. slightly opalescent; Wb. opalescent.

August, 1923: Blood Wassermann negative; C.S.F. Wassermann 0-0-0; cells 31, N.A. slightly opalescent, mastic: very strong paretic curve.

September, 1923. Blood Wassermann negative, C.S.F. Wassermann 0-0-2; cells 19, N.A. slightly opalescent, mastic: typical lues cerebri curve.

October, 1923. Blood Wassermann negative; C.S.F. Wassermann 0-0-0; cells 43; N.A. slightly opalescent; mastic: lues cerebri curve.

November, 1923: Blood Wassermann negative; C.S.F. Wassermann 0-0-0; cells 6; N.A. slightly opalescent; mastic: weak paretic curve.

December, 1923: The patient had improved enough to be discharged, though he still exhibited considerable defect

November, 1924. Readmitted because of excitability, profanity and theft. Blood Wassermann negative; C.S.F. Wassermann 0-1-2; cells 120; N.A. slightly opalescent; mastic: very strong paretic curve.

April 29, 1925: After progressive deterioration the patient began to have convulsive attacks which continued at frequent intervals until his death on May 1, 1925.

Histological.—This case presents the usual paralytic changes of very severe degree, marked architectural disturbance and loss of nerve cells, strongly infiltrated vessels, numerous cells breaking through into the nervous tissue, strongly proliferated microglia and rather intense iron reaction in the microglia and walls of the blood-vessels.

Case 44 (Tho.).—On admission, May 22, 1922, the patient was confused and excited. Blood Wassermann negative (Stern +++); C.S.F. Wassermann 1-3-3; cells 67; N.A. +; Wb. ++, mastic: strong paretic curve.

June 2, 1922: Inoculated with tertian malaria, seven rises of temperature

July 2, 1922: Blood Wassermann +, (Stern +++); C.S.F. Wassermann 0-0-2, cells 36; N.A. +; Wb. ++.

August, 1922: C.S.F. Wassermann 1-3-3; cells 30; N.A. ±, Wb. +.

September, 1922; Blood Wassermann negative; C.S.F. Wassermann 0-1-1, cells, 22; N.A. ±; Wb. ++.

October, 1922. Blood Wassermann negative, C.S.F. Wassermann 0-0-1, cells 42; N.A. ±; Wb. ++. The patient was discharged in a good remission.

December, 1923: Readmitted confused and excited.

April, 1924: The patient had become considerably demented and wholly indifferent, and was having light convulsive attacks which continued until death in status paralyticus, September, 1924.

Histological.—The parenchymatous changes (architectural disturbance and loss of nerve cells) is only of moderate severity. The infiltration, too, is slight, except for a thick lymphocytic ring around an occasional larger cortical vessel. The iron content of the blood-vessels and of the microglia is small, but the microglia is strongly proliferated.

Case 45 (Bec J.).—On admission, August 4, 1920, he was confused, and evidenced considerable mental impairment. Blood Wassermann +++ C.S.F. Wassermann 3-3-3; cells 32; N.A. ++.

August 20, 1920. Inoculated with tertian malaria; fourteen rises of temperature.

October, 1920. He had improved slightly, was helping about the ward, though quite without insight into his illness.

February, 1921: Condition essentially the same. Blood Wassermann + +; C.S.F. Wassermann 1-3-3; cells 13; N.A. + +, Wb. + +.

June, 1922: The patient was indifferent, euphoric, and had occasional convulsive attacks. He continued slowly downhill and having attacks, in one of which he died, July, 1925.

Histological.—Infiltration is very slight, both in meninges and in the perivascular spaces of the cortex. The glia is little proliferated. The quantity of iron in the walls of the blood-vessel and macroglia is small. The arrangement of the ganglion cells and of the cortical layers is rather well preserved, but there is considerable loss of cells. In all areas the ganglion cells show severe "acute swelling."

As previously mentioned, in such cases as these ("Anfallsparalyse") one expects to find changes of a rather unusual sort, deviating considerably from the common picture of general paralysis and occupying a special position as regards the frequency with which spirochætes may be found.

In the first place spirochætes were found in only one of the six cases. Every case died during an epileptic attack and according to Jahnel [13] these are just the cases in which spirochætes should be present in great numbers. He says that: "During the chronic course of the disease there occasionally appear acute exacerbations, which we designate as paralytic attacks. It is not seldom that death takes place in a paralytic attack. Anatomically, corresponding to this 'attack' there is a sudden and massive destruction ('Untergang') of nervous tissue; parasitologically, a strong and widespread proliferation of spirochætes in the brain. The death in a paralytic attack is not only a 'brain death' but also a 'spirochætal death'; we have before us one of those cases in which the agent of syphilis is the direct cause of death." Jakob [15] agrees with Jahnel, in that the attack corresponds to a strong and widespread proliferation of spirochætes, and Hermel [9] was able to find them in 80 per cent. of such acute ("Anfallsparalyse") cases. Others, as Marinesco and Minea [26], Levaditi, Marie and Bankowski [24], have also emphasized the richness of spirochætes in cases dying soon after or in attacks. In explaining the failure to find spirochætes in such cases, he says (p. 35): "It seems quite intelligible that in such cases spirochætes may not be found, especially when the interval between the attack and death is more than a few days (two to

three)," that is to say, that during such an interval the antibodies called forth by this very massive proliferation of spirochætes may be able to destroy the agent of the attacks.

All of these patients showed the acute exacerbations, such as, according to Jahnelt's explanation, correspond to a massive proliferation of spirochætes and, as they died in the attacks, there was no interval during which the activity of the antibodies might destroy the spirochætes and thus account for the failure to find them. One case of course died three weeks after treatment, which may or may not be held responsible for the inability to find spirochætes. On the other hand, the last five cases died at intervals of eight months to five years after treatment, and it is hardly conceivable that any influence of the treatment on the spirochætes could be manifested after such a long time, and, as will be pointed out, in these cases the spirochætes apparently may begin to proliferate again after six months.

These cases would then seem to lend more support to the theory of Ehrlich [3], that these acute exacerbations are due to a rapid absorption of endotoxins liberated by a sudden massive destruction of spirochætes by antibodies ("thus the apparent paradoxical findings, death without spirochætes"), and to the views of Hauptman [7], who also regards the paralytic attacks as clinical manifestations of destruction of the spirochætes by the antibodies, the resulting toxin producing a clinical picture comparable to an anaphylactic shock. Nor are these latter theories necessarily refuted by the frequency with which spirochætes have been found in such cases by many authors. It is conceivable that the finding, or the failure to find, spirochætes might depend upon whether or not, at the time of examination or death, the antibodies had succeeded to a certain degree in the destruction of the spirochætes. In either case one might expect convulsive attacks, until the spirochætes become so reduced in number or virulence as to constitute no longer a stimulus to the formation of antibodies, or else that the body loses its power of reacting to this stimulus. Jahnelt, although denying an important rôle to the endotoxins in producing these severe clinical manifestations, does attribute the failure to find spirochætes in such cases to their destruction by antibodies, although he is of the opinion that the attacks tend to appear before the antibodies become of importance.

The next point is the degree of mesenchymal proliferation present in these cases. Jakob [15] stresses the frequency of miliary gummata, or gummatous changes in the blood-vessels, in the usual cases of general

paralysis, especially in those with many acute exacerbations leading rather rapidly to death, the so-called "Anfallsparalyse." Among fifty such cases he found gummatous changes of the blood-vessels in twenty-two. He also emphasizes the frequency of severe endarteritic changes. In only one of these six cases, however, did some of the vessels present marked mesenchymal proliferation, which may possibly represent the early stage of a developing gumma. In only one case were marked endarteritic changes of the small cortical vessels found. These six cases can, of course, offer no refutation to the assertion of Jakob, that the reaction of the mesodermal tissue in such cases is unusually strong, since his conclusions are based on the study of fifty cases. It is conceivable, accepting his conclusions to be correct, that the failure of such a reaction in these cases may be related to the malarial treatment. They all, with the exception of one case, show very severe changes, and contrast sharply with the other cases (according to interval after treatment), and so seem to justify their being regarded as a distinct group.

In considering the alterations in the histological picture that may follow malaria, and possibly may in part be due to some change in the relationship between the parasite and the reactive ability of the body brought about by this treatment, two other cases may be briefly described, which show a reaction quite different from those previously considered. These are two cases with syphilitic endarteritis of the small cortical vessels and their clinical courses are as follows:—

Case 46 (Bod.).—Admitted April 2, 1922. His symptoms dated back four years. Commencing with headaches and irascibility, he later began drinking heavily, and was at times confused and expressed expansive ideas. His pupils were unequal and reacted sluggishly to light, the left side of his face was weak, and his tongue deviated to the left. Blood Wassermann +; C.S.F. Wassermann 3-3-3, cells 132; N.A., +.

In May, 1922, he was inoculated with tertian malaria, and had three rises of temperature.

October, 1922: He had improved sufficiently to be discharged.

December, 1922: In another hospital, he was twice inoculated with malaria, having one and five rises of temperature respectively. Following this there was some clinical improvement. March, 1923: Blood Wassermann +++ , C.S.F. Wassermann 3-3-3.

Towards the end of 1924 he commenced expressing paranoid ideas, was resistive and refused nourishment. Later he developed pneumonia, and died March 14, 1925.

Case 47 (Rie.).—Admitted April 13, 1921. For one year he had shown emotional instability, poor memory, irascibility and some confusion. On

admission he was indifferent, wholly without insight, at times profane and had considerable disturbance of speech. Pupils were unequal and reacted sluggishly to light. There was right-sided facial weakness. Blood Wassermann +++ ; C.S.F. Wassermann 3-3-3; cells 37; N.A. ++; Wb. +++.

July, 1921: Inoculated with tertian malaria, six rises of temperature.

No improvement followed. He continued indifferent and manifested increasing dementia, becoming finally apathetic. April, 1925: Blood Wassermann +++ ; (Stern, ++++), C.S.F. Wassermann 0-1-2; cells 8; N.A. slightly opalescent, Wb. opalescent; mastic: typical lues cerebri curve. He died September 9, 1926.

Histologically the two cases are very similar. The meninges show considerable connective tissue thickening, but little infiltration. The cortical architecture is fairly well preserved in spite of a rather marked falling out of ganglion cells. The cortical perivascular infiltration is that of general paralysis, but is of a very mild degree. Most striking are the changes in the small vessels themselves. There is a fibrous tissue thickening, with marked increase of nuclei, and on cross section one sees a thick wall and a very narrow lumen. The vessels coursing down from the meninges appear as streaks of connective tissue, rich in nuclei, and often very tortuous. The nuclei in these cases for the most part are small, deeply stained and often pycnotic. This probably indicates that these changes are not of very recent date, at least in many cases of syphilitic endarteritis [Jacob (16)] the endothelial and adventitial cells appear more progressive than regressive. There is considerable proliferation of macroglia, rich in protoplasm and often bunched together in tufts. On the other hand the microglia is little proliferated and the typical rod-shaped cells are almost entirely absent. The iron content of the walls of the blood-vessels and of the microglia is very slight.

In reviewing these cases there is obviously no parallelism between the clinical course and the pathological findings in the brain. Even the cases with slight changes did not differ clinically from those with very severe changes. That such inconsistencies occur in general paralysis is well known. In 1904, Alzheimer [1], in his classical work on general paralysis, described the severest parietic changes in a case committing suicide before any symptoms appeared. Similar observations have since been recorded. It is generally accepted that there is no real parallel between the intensity of inflammation and the severity of parenchymatous changes.

This is not surprising if the parenchymatous changes be regarded as degenerative incident to the presence of spirochaetes in the body, whether a direct injury by the spirochaetes themselves or by some indirect toxic influence, and the inflammation as indicating the reaction of the body to the invader. In the cases with slight changes it would seem that

the subsiding inflammation is due to the fact that the invader has been destroyed, or at least so reduced in numbers (in only one case in twenty-nine were spirochætes found) as no longer to constitute a stimulus to the defensive mechanism of the body. The spirochætes, however, have so altered the metabolism of the nerve-cells, or in their reduced numbers continue to give rise to toxins to the extent of obviating functional recovery, despite the fact that considerable restitution has taken place in the arrangement of the cortical layers and nerve-cells.

In comparing the pathological findings with the serological reactions, there also appear some inconsistencies. The relationship among the ten cases studied pathologically one to two-and-a-half years after treatment, is very striking. In the five cases in which the histological changes were slight there was improvement serologically, whereas the five cases with severe changes had in general no alteration of the reactions, or else it became worse. In contrast with this, of the three cases examined three to five years after treatment, in one with severe changes there was some improvement, and in another with less severe changes the serology was very slightly worse after treatment. Among the six cases characterized by epileptic attacks, there is no apparent relationship between severity of histological changes and the degree of alteration of the reactions. Is it merely a coincidence that the serological alterations in the ten cases studied one to two-and-a-half years after treatment tend to run parallel with the severity of the inflammatory reaction, or is it possible that a stationary condition, or an increased intensity of the serological reactions, may be taken as an indication of a still active inflammatory process? Were the latter the case, then very interesting relationships become obvious. An improvement in the serological reactions would indicate a standstill or regression of inflammation, following the destruction of the spirochætes. (I refer to the almost negligible spirochætal findings in such cases—one case in twenty-nine.) That clinical improvement does not coincide in some cases may mean that, although the spirochæte has been eliminated, the disturbance to cell metabolism has been so severe that functional recovery is no longer possible. In such cases renewed therapeutic efforts would be of no avail. On the other hand, if there has been no improvement in the serological reactions up to six months or longer, it would indicate the presence of spirochætes which, as my cases seem to indicate, may after six months cause a new flare-up of inflammation. Such cases might be benefited by renewal of treatment. It is, of course, impossible to

formulate any definite conclusions from such limited observations, but they suggest at least a possible correlation between the histological process and the serological reactions.

One of the most striking serological reactions is the mastic. Kirschbaum and Kaltenbach [19, 22] have attached a prognostic value to it. They noted that it often changes to a lues cerebri type of curve on improvement, and when the patient becomes worse it shifts back towards the general paralytic type. Among the cases I examined the mastic reaction was studied in only sixteen, and, unfortunately, in these cases not frequently enough to permit very definite conclusions. Nevertheless, certain relationships stand out which seem deserving of mention. In only one case among those showing histological improvement was the mastic reaction studied after six months. In this case the reaction became weaker, and approximated the lues cerebri type. Averaging the curves of all the cases for each period after treatment, it was possible to construct a curve (fig. 17). It is at least interesting that this curve runs almost parallel with the severity of the histological changes. Between four to fourteen days it takes up a position even more typical for general paralysis than before treatment. Between three to six weeks it shows a precipitant drop, and, except for a slight secondary rise, remains at this low level until the period six to nine months is reached. After six months it shows a very marked ascension, reaching a level slightly more typical for general paralysis than before treatment. Thus it is seen that this tremendous secondary rise corresponds to the period where a new flare-up of inflammation may take place.

Another serological reaction to which considerable importance has been attached is the hæmolysin reaction of Weil and Kafka [38,39]. These authors consider that it indicates an increased permeability of the meningeal blood-vessels, and found it positive in most cases of general paralysis. Potzl [29] found it disappearing after malarial treatment, generally after about two months. Horn's [11,12] investigations were essentially in confirmation. Hauptmann [8] sees in these observations evidence in support of his hypothesis that the nervous tissue is injured by substances escaping from the blood through the meningeal blood-vessels, which are rendered more permeable as a result of injury by toxins incident to the presence of spirochætes in the body.

Spatz and Metz (31,32) have made an extensive study of the iron reaction in the brain and have called attention to the diagnostic value of its presence in the microglia in general paralysis. They also found considerable iron in the walls of the blood-vessels, and a striking

parallelism between this and the iron content of the microglia. They concluded that the iron in the microglia was of hæmatogenous origin and thus that in general paralysis the blood-vessels are more permeable. My findings are in keeping with these. Directly after malarial treatment there is a great increase of iron in the blood-vessels and microglia; after three to six weeks, with the improvement in the histological picture, the iron content rapidly diminishes. These observations seem to indicate an increased permeability of the blood-vessels during and directly after treatment, and then a rapid approach towards normal.

Hoff and Silberstein [10] have found an increase of the opsonic index for streptococci, staphylococci and colon bacilli in the blood and spinal fluid of patients during malarial treatment, and although their results with spirochætes were not satisfactory, nevertheless there was some evidence that they may be taken up by phagocytic cells. Furthermore, the spirochætes treated with spinal fluid and leucocytes of these patients soon disintegrated and produced no testicular lesions in rabbits, whereas when spinal fluid and leukocytes of untreated patients were employed the spirochætes retained their motility and produced typical syphilitic lesions.

I may recall here the presence of many macrophages in the meninges soon after the end of the fever. This may be an histological expression of increased phagocytic power. Sträussler and Koskinas [36] also noted numerous macrophages in the meninges directly after treatment.

SUMMARY AND CONCLUSIONS.

(1) In sixteen cases coming to post-mortem within six weeks after malarial treatment, the histological changes may be described as a severe diffuse general paralytic process. Outstanding is the strong glial proliferation and the richness of iron in the walls of the blood-vessels and microglia. The increase of iron probably indicates an increased permeability of the blood-vessels. The presence of numerous macrophages in the meninges may be the expression of an increased phagocytic power, evidence of which has been found in studies on the cerebrospinal fluid by others. Spirochætes were found in one case.

No evidence was found indicating a change to a more specific type of reaction. In the earliest stages only was a considerable predominance of lymphocytes in the meninges present, whereas in the cortical perivascular spaces plasma cells predominated throughout.

Towards the end of this period the infiltration tends to increase on the arterioles and venules and decrease on the capillaries.

(2) Following this period of exacerbation of inflammation there is a period of restitution. In thirteen cases, after six weeks and up to two-and-a-half years, there is a gradual improvement in the arrangement of the cortical layers and nerve-cells, and at the same time a rather rapid and considerable reduction of infiltration and of glial proliferation.

The very considerable reduction of iron in blood-vessels and microglia adds support to the serological evidence of a decrease in the permeability of the blood-vessels.

During the interval one to two-and-a-half years there is a secondary increase of macrophages in the meninges, of microglia, and of iron in the walls of the blood-vessels and in the microglia. In none of these cases were spirochaetes found. The fact that in the twenty-nine cases thus far considered spirochaetes were found only once, suggests strongly that the malarial treatment has brought about a tremendous destruction of them.

(3) Among the cases coming to autopsy from six months to two-and-a-half years after treatment, six are characterized by scattered foci of intense inflammation in which the mesodermal tissue is strongly proliferated, even to the formation of typical miliary gummata in one. Spirochaetes were found in five of these six cases. It seems probable that these are cases in which the invader was not successfully exterminated, and after six months is again able to regain its virulence and to proliferate.

In considering the serological reactions of these cases it is found that no improvement followed treatment, whereas in the cases with histological improvement there was also serological improvement. This suggests the possibility of recognizing the cases in which extermination of the spirochaetes has not been successful, and therefore the liability of a secondary flare-up of the process. Such cases might benefit by a new therapeutic effort.

(4) Three cases, three to five years after treatment, follow less clearly the above rules. This may be taken to mean that any influence of the malarial treatment has been lost after three years.

(5) Six cases are described that were characterized by frequent convulsive attacks, and which died in such attacks. The above findings cannot be correlated with these cases. It seems likely that they may represent a special group.

(6) Two cases of syphilitic endarteritis of the small cortical vessels were found among the forty-seven examined, suggesting that as a result of the malarial treatment the general paralytic process may, in an occasional case, be replaced by such a reaction.

(7) In one case which terminated during a remission the histological picture was that of "stationary paralysis."

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INCREASED INTRACRANIAL PRESSURE.

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INTRODUCTION.

IN recent years a considerable advance has been made in our knowledge of the factors influencing intracranial tension, but there still remain many problems connected therewith which require elucidation. Until more complete information is available with regard to the factors which determine the normal intracranial pressure, it remains difficult to ascertain precisely the mode of causation of such an abnormal condition as increased intracranial tension. Nevertheless, careful investigations of pathological states must stimulate research upon the outstanding anatomical and physiological difficulties, and may even throw considerable light upon these problems.

Reference to the anatomical position and circulation of cerebro-spinal fluid within the cranium shows that its pressure must be the same as intracranial pressure, and therefore it is possible to express intracranial tension in terms of cerebro-spinal fluid pressure. The cranium being practically a closed box, any alteration of intracranial tension must be due to a change in one or more of the three elements—brain, blood and cerebro-spinal fluid—which it contains. The experimental work of Weed and his co-workers has shown that variation in one content may, within certain limits, be compensated for by modification in the volume of one or both of the others. Dixon and Halliburton [3] corrected the opinion expressed by Leonard Hill [5] that the cerebro-spinal fluid and cerebral venous pressures were the same. These observers showed that the cerebro-spinal fluid pressure was influenced passively, to a slight extent, by alteration of the arterial and venous pressure, but that this influence was trivial compared with the much greater changes which resulted from an increased production of the fluid. Dixon and Halliburton further demonstrated that an alteration of the cranial venous pressure produced a similar, but not identical, alteration in the cerebro-spinal fluid pressure, and conversely an increase

in the latter pressure caused passively a slighter rise in the cranial venous pressure. Weed and Hughson [15] have confirmed these results and proved in a large series of experiments that in almost every case the cerebro-spinal fluid pressure was considerably higher than that of the pressure in the hinder part of the superior longitudinal sinus. Although it seems now definitely established that the cerebro-spinal fluid pressure is higher than the venous pressure in the sinuses, which have strong walls and can therefore withstand considerable pressure, it is not legitimate to assume, as Brain [1] has pointed out, that the pressure in the small cerebral veins is as low as that in the large intracranial sinuses. It appears highly improbable that the pressure in the thin-walled and poorly supported cerebral veins is less than the fluid pressure, because if this is the case it is difficult to understand how the cerebral veins can remain patent and avoid being compressed by the higher pressure around them. Most of the superior cerebral veins pass obliquely forward to pour their contents into the superior longitudinal sinus against the flow in the sinus. This will have the effect of raising the pressure in the veins above that in the sinus, and the arrangement, which otherwise seems a very curious one, may well be for this purpose, and illustrates once again the inter-relationship of function and structure.

The intracranial arterial pressure is also under normal circumstances a factor in the maintenance of cerebro-spinal fluid pressure, but it has been shown that a sudden and considerable alteration in the arterial pressure is required in order to influence appreciably the pressure of the fluid. While it is clear that the cerebro-spinal fluid pressure is dependent upon the intracranial arterial and venous pressures, and may be modified by changes in one or the other, it appears to be more independent of both than many of the earlier observers realized. Weed [14] has stated that "the pressure of the cerebro-spinal fluid may be considered to be relatively independent of both, in that normally it maintains an individual fairly constant level below that of the intracranial arteries and somewhat above that of the intracranial veins." For reasons emphasized by Brain and already mentioned, it would be more accurate to substitute large intracranial sinuses for intracranial veins, in the above statement. There is evidence [15, 16, and 17] that the fluid pressure may be altered independently of any change in the intracranial and systemic vascular pressures. Furthermore, from observations in the experimental production of internal hydrocephalus and from other studies, it is evident that the cerebro-spinal fluid may still be produced when the intraventricular pressure

has been considerably raised above the normal. We do not as yet know whether the cerebro-spinal fluid is a secretion or of the nature of a dialysate, but evidence seems to be accumulating in favour of the latter. Provided the composition of the plasma remains constant, it has been shown that the rate of production varies directly with the capillary pressure, and that this is dependent more upon venous than upon arterial blood-pressure.

RAISED INTRACRANIAL TENSION.

The establishment of the greater independence of the cerebro-spinal fluid pressure has been stressed because it seems to be of importance when we refer to such an abnormal condition as the increased intracranial tension which is so frequently associated with a tumour within the cranium.

It is difficult to believe that the introduction of an additional mass within the closed box can *per se* be the cause of the raised tension, since a large frontal tumour may fail to produce it, whereas a small one in the subtentorial region may cause profound manifestations of increased intracranial pressure. It is not easy to understand why the three normal contents of the cranium should be able to compensate for the introduction of an additional mass in certain sites and not in others, but it would appear that in certain positions the tumour is able to affect one or more of the contents in such a way as to upset the conditions upon which normal tension depends. Unfortunately, we do not yet know precisely the factors which determine the normal cerebro-spinal fluid pressure, which Weed has estimated as equal to 110 to 130 mm. of Ringer's solution. Weed [15] thinks the normal pressure "may be largely determined by the balance between the constant new production within the cerebral ventricles and the absorption into the dural sinuses: this pressure of the cerebro-spinal fluid becomes dependent also upon intracranial, arterial and venous pressures, not only because of the relation of these latter pressures to the production and absorption of the fluid, but because of the constancy of volume of the intracranial contents."

From these introductory references it will be appreciated that it is unlikely that any change in the pressure in the intracranial sinuses or arteries could cause the great elevations of intracranial pressure which are not unfrequently associated with cerebral tumour. The profound and early evidence of raised intracranial tension occurring with subtentorial growths might suggest the possible compression of the lateral

sinuses as they leave the cranial cavity through the jugular foramen. It might be thought that such obstruction would induce a pressure in the superior longitudinal sinus greater than the cerebro-spinal fluid pressure, and so delay the absorption of the fluid and lead to its accumulation within the cranium, with consequent increase of tension. It is quite clear, however, on anatomical grounds, that such a rise of pressure in the sinuses could only be of very short duration on account of the presence of numerous emissary veins which would provide a collateral drainage and rapidly reduce the venous pressure.

On reviewing the three contents of the cranium and their relation to one another, it appears most probable that the tumour raises intracranial tension through the cerebro-spinal fluid. There are also indications that in cases of increased intracranial pressure the cerebro-spinal fluid is commonly present in larger quantities than in the normal cranium. The excess may be in the subarachnoid space, in the ventricles, or in both these positions, and its situation will be more fully discussed later. Such an increase in the amount of fluid beyond a point at which it might be compensated for by the other cranial contents would obviously raise intracranial tension, and could be created either by excessive production, interference with absorption, or obstruction somewhere between the sites of its production and absorption.

Before discussing these three possible disturbances of the balance which normally exists between the production and absorption of cerebro-spinal fluid, it is more convenient to refer to the factors which appear to influence the occurrence or absence of raised intracranial pressure in cases of tumour. From an analysis of large numbers of patients suffering from intracranial tumour, it is generally agreed that the anatomical site of the growth is of first importance with regard to the occurrence of increased tension. The rate of growth and size of the tumour also seem to play some part, but they appear to be of distinctly less significance than the anatomical situation. The presence or absence of œdema of the nervous tissue round the tumour needs consideration, but it cannot be of such primary importance as the site of the neoplasm, as there is no reason why œdema should occur earlier and more constantly in one position than in another. When œdema does supervene, it must add to the mass within the cranium and thus, like the size of the tumour, constitute a factor which must bear on the problem. However, as œdema may develop round a tumour in any position, it cannot be regarded as of the same significance and importance as the site of the growth.

The histological character of the growth bears no relation to the occurrence or absence of increased intracranial pressure. Since the site of the tumour is the factor of primary importance, it is likely that the causation of the raised pressure must be of mechanical origin. The influence of the rate of growth, size of the tumour and possibly the occurrence of œdema, is also compatible with a mechanical origin, since a slow-growing or small growth would often permit some compensation for the mechanical disturbance to take place, which is less possible for a rapidly increasing in size, or surrounded by a considerable

Returning to the question as to whether tumours in certain situations can interfere with the absorption of the cerebro-spinal fluid, obstruct its flow or cause an increase in its production, the first of these possibilities may now be considered. Recent research [12 and 13] has provided considerable knowledge regarding the absorption of cerebro-spinal fluid through the arachnoid villi into the venous sinuses. In view of this information it is difficult to see how a tumour could affect the drainage of the fluid, and impossible to understand how a growth in the mid-brain or subtentorial region could interfere with absorption.

obstruction to the venous drainage from the choroid plexuses can induce an excessive production of cerebro-spinal fluid: consequently it seems necessary to consider further whether the raised intracranial pressure associated with brain tumour is caused by excessive production of cerebro-spinal fluid due to venous obstruction, and this will be discussed in detail when a fuller reference has been made to the position and relations of the great vein of Galen.

Before this is done it is necessary to mention the third possible cause of the raised pressure; viz., obstruction at some point to the normal flow of cerebro-spinal fluid. It is well known that tumours in certain situations, particularly those in the posterior fossa of the skull, may induce distortion and displacement of the brain-stem. This has been thought by many to lead to obstruction of the flow of cerebro-spinal fluid through the narrow aqueduct of Sylvius, which will readily cause dilatation of the lateral and third ventricles, and so explain the ætiology of increased intracranial pressure. Since subtentorial growths are most constantly manifested by signs of increased pressure at an early date and are most likely to bring about distortion and displacement of the brain-stem, this possibility must also be considered in connection with its clinical and pathological findings.

GREAT VEIN OF GALEN.

The two veins of Galen which pass backwards in the velum interpositum are each formed by the vein from the choroid plexus of the lateral ventricle and the vein of the corpus striatum. The latter receives small tributaries from the wall of the anterior horn of the ventricle and the septum lucidum; whilst lying in the velum interpositum the veins of Galen receive blood from the choroid plexuses of the third ventricle and are joined by several small veins from such structures as the corpus callosum, quadrigeminal bodies, and optic thalami, and may receive one large venous channel named the basilar vein. The basilar vein is formed by the anterior cerebral vein, the deep Sylvian vein, and the inferior striate veins which emerge through the anterior perforated spot. After curving round the midbrain, where it receives numerous small branches, the basilar vein either joins the vein of Galen of its own side, the great vein of Galen, or the straight sinus. When it is a tributary of the vein of Galen, the junction occurs exactly at the point where the two veins unite to form the great vein of Galen. The great vein of Galen, as explained in an earlier paper [11] does not take a direct course to the straight sinus, but curves

round, and is throughout in intimate contact with the splenium of the corpus callosum. Thus, from its origin, the vein passes at first backwards and upwards, and then forwards and upwards, to reach the hinder end of the inferior longitudinal sinus (fig. 1). The relation with the splenium is always most intimate, and the vein opens into the sinus like the tributaries of the superior longitudinal sinus—e.g., against the flow of the current in the sinus. Taking this course, which is much more vertical than horizontal, it will be at once noticed that anything which raises the tentorium is certain to exert tension upon the vein and

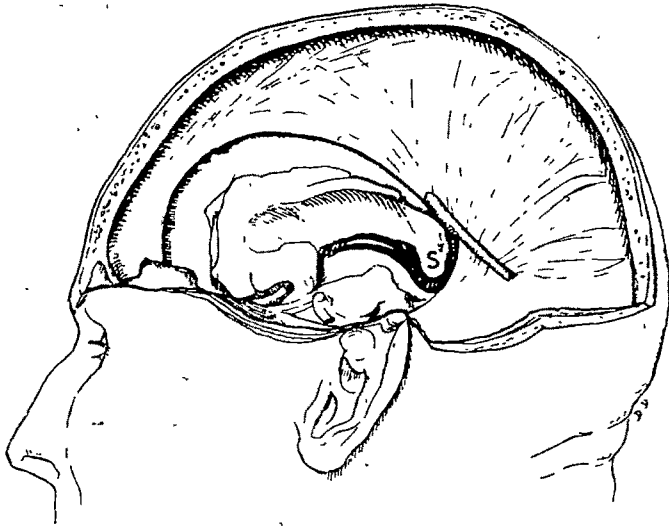


FIG. 1.—Drawing of dissection to show the relation of the great vein of Galen to the splenium. Part of the inferior longitudinal and straight sinuses have been incised to display the termination of the vein. S. = splenium.

cause it to be compressed against the splenium. It is important to remember that the tentorium may be elevated directly, as by pressure from below, or indirectly, as from lateral deflection of the falx cerebri, owing to the mode of attachment of this structure to the tentorium. The course and relations of the great vein of Galen are not represented in many of the modern anatomical textbooks, but are figured, as I have described, in several of the older volumes. They are well shown in many of the plates published in the classical memoir by Key and Retzius [9] and can be demonstrated in a dissection made from the side, without disturbance of the falx cerebri or tentorium. Cutting of these partitions, as customary in the usual method of removal of the brain, destroys the correct relations and general course of the vein.

The great vein of Galen, in addition to the basilar vein which may empty into it, receives some of the superior cerebellar veins, and also veins from the hinder and medial surface of the cerebrum. Compression of the great vein of Galen would undoubtedly obstruct the flow into it from these cerebellar and cerebral veins, but efficient compensation would be possible through venous communications; which are known to be free in the case of both superficial cerebral and cerebellar veins. These communications would probably prevent any permanent passive congestion of the cerebrum or cerebellum, but would obviously not relieve the engorgement of the tributaries from such structures as the choroid plexuses, as the obstruction is in front of the junction of these cerebral and cerebellar veins with the great vein of Galen. When the basilar vein joins the great vein of Galen or the straight sinus, compression of the great vein of Galen against the splenium would clearly prevent the basilar vein from relieving passive engorgement of the radicals of the veins of Galen, including the veins from the choroid plexuses of the third and lateral ventricles. When the basilar vein opens into the veins of Galen, the junction is always found just at the point where these two fuse to form the great vein of Galen, and their orifices are in such a position that partial occlusion at least would appear inevitable when the great vein was pressed upwards against the splenium; in fact, it is likely that with elevation of the tentorium the vein would initially be compressed at this point. Therefore, wherever the basilar vein terminates, it seems quite impossible for it to compensate satisfactorily, as regards the venous drainage from the choroid plexuses, for obstruction to the flow in the great vein of Galen. Thus, on anatomical grounds, compression of the great vein of Galen by elevation of the tentorium, either directly by pressure from below, or indirectly by deflection of the falx cerebri, does seem a reasonable possibility. Such an obstruction will impede the venous return from the choroid plexuses and cause an increased capillary pressure in them. This condition would induce an excessive production of cerebro-spinal fluid, since investigations have proved that the rate of formation of the fluid varies with the capillary pressure in the choroid plexuses. There is no doubt that deflection of the falx can and does occur commonly in association with supratentorial growths and particularly with those in the more posterior part of the cerebral hemisphere, and there is no doubt that such deflection will elevate the tentorium. There may, however, be some hesitation in accepting the suggestion that subtentorial growths can raise by pressure from below such a strong structure

as the tentorium. Investigations of the shape of the ventricles in cases of intracranial tumour have recently indicated that elevation of the tentorium by growths below it is a possibility. Elsberg and Silbert[4], by the study of ventriculograms and casts made of the ventricles from post-mortem specimens, have recently demonstrated some very significant points. In subtentorial growths they found that the lateral ventricle on the side opposite to the growth was regularly more dilated than that, on the same side, and that the posterior horn on the side of the tumour was consistently shorter and displaced forwards and outwards, when compared with the opposite side. Such displacement by growths in the posterior fossa can only be produced by elevation of the tentorium. Such a contention is supported by a further observation which they record, that in hydrocephalus associated with subtentorial tumours the cavity of the descending horns of the lateral ventricles (the part of that cavity situated immediately above the tentorium) was often relatively small compared with that of the anterior horns and bodies of the ventricles. Although not invariably found, this second observation by Elsberg and Silbert can only be regarded as further evidence of the possibility and the actual occurrence of elevation of the tentorium by some growths in the posterior fossa. These observations upon the size and form of the lateral ventricles on the two sides are confirmed by an example of cerebellar tumour which was kindly brought to my notice recently by my colleague, Professor J. Shaw Dunn. In this specimen the displacement of the posterior horn and the smaller size of the descending horn on the same side as the tumour are strikingly shown.

TUMOURS ABOVE AND BELOW TENTORIUM CEREBELLI.

Having considered the exact position and communications of the great vein of Galen, it is now convenient to discuss more fully the evidence upon which to decide on the relative importance of the two possible causes of raised intracranial pressure, the two being:—

- (1) Obstruction to the venous return from the choroid plexuses, with a consequent increased production of cerebro-spinal fluid, and
- (2) Displacement and distortion of the brain-stem inducing obstruction to the flow of cerebro-spinal fluid through the aqueduct of Sylvius, which must in turn lead to dilatation of the lateral and third ventricles.

Since the tentorium almost divides the cavity of the cranium into two parts, the communication provided by the hiatus tentorii being largely occupied by the midbrain, there is considerable advantage in

studying, in the first place, the influences of supra- and infra-tentorial tumours separately. The supratentorial subdivision of the cranial cavity is partially divided into two by the falx cerebri. This partition, being sickle-shaped with its apex in front, separates completely the mesial surfaces of the two occipital lobes behind, while in front of its attachment to the tentorium a large communication between the two halves of the supratentorial part of the cranial cavity is left. This opening is more or less oval in shape, with its long axis antero-posterior and its vertical extent greatest in the frontal and parietal regions (fig. 1). Through the opening pressure can be transmitted across the

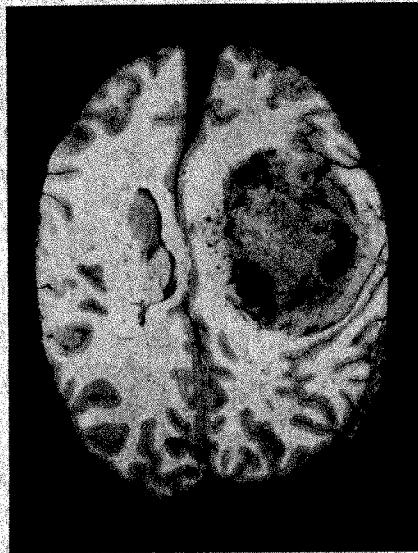


FIG. 2.—To show how a supratentorial tumour can deflect the falx.

middle line without deflection of the falx. Such pressure would be produced most likely by tumours in the lower part of the frontal and parietal lobes, and might conceivably displace the brain-stem very slightly to the opposite side and possibly downwards. It is conceivable, but not very likely, that this pressure would be sufficient to cause serious obstruction to the flow of cerebro-spinal fluid through the aqueduct. Any downward displacement would be quite as likely to cause tension upon, and so diminish the lumen of, the great vein of Galen. It is difficult, if not impossible, to believe that tumours in any other part of the supratentorial space can seriously displace the brain-stem. On anatomical grounds, such displacement seems most unlikely

to arise from growths in the occipital and hinder part of the parietal lobes, and yet it is tumours in these two situations above the tentorium which most frequently cause symptoms of raised intracranial pressure. Tumours placed in front, above, and particularly behind the opening below the falx, are liable to cause deflection of this fold to the opposite side, a condition quite commonly seen at a post-mortem examination (fig. 2). Of course it is only possible for this to occur when the tumour has grown to some size. Observing the falx from the side, it will be noticed that the risk of deflection is greater as we pass backwards from the frontal to the occipital regions, since the extent of the falx exposed to the hemisphere increases. The risk is greater in the occipital region than in any other position. With reference to this, it is interesting to recall the incidence of absence of symptoms of intracranial pressure in the fifty-nine cases spoken of in an earlier part of the paper. In tumours of the frontal and fronto-parietal regions there was no evidence of increased pressure in a third, in the parietal lobe in a fourth, in the temporo-parietal and temporo-occipital regions in a fifth; while in the nine cases of tumour of the parieto-occipital region, only one failed to exhibit signs of intracranial pressure, and the only patient without symptoms, in the series of five tumours of the occipital lobe, requires further explanation, which probably accounts for the absence of pressure symptoms. This patient died from a hæmorrhage in the opposite cerebral hemisphere, and at the time of the occurrence the occipital tumour was small; it is therefore evident that this patient died from cerebral hæmorrhage at an early stage in the development of the tumour, and before it had grown sufficiently to induce symptoms of raised intracranial pressure or to cause any deflection of the falx.

These figures certainly seem to establish a definite relationship between the frequency (of the appearance) of signs of intracranial pressure and the risk of deflection of the falx. On the other hand, they do not seem to denote any relation between the occurrence of pressure symptoms and the possibility of displacement or compression of the midbrain, and such an association seems very improbable, as the frequency of symptoms is greatest in tumours of the hinder part of the parietal and occipital lobes, in which regions the midbrain is most effectually protected from pressure by the broader part of the falx.

In a series of cases published by Brain [1], in which the site of the tumour was verified at operation or post-mortem examination, similar deductions may be made, and all other reports in lists of supratentorial tumour which I can find manifest this association of the

frequency of symptoms of raised pressure within the cranium, and risk of deflection of the falx. The records from cases where combined ventricular and lumbar punctures have been taken also show that any obstruction of the aqueduct associated with supratentorial tumours is exceedingly rare. Recently Hodgson [6] investigated twenty-one patients suffering from tumours above the tentorium and found that there was only evidence of block in one, which was a case of pinealoma. Consequently it does not seem possible to believe that displacement or torsion of the midbrain can be an important factor in the etiology of raised intracranial pressure in supratentorial growths, whereas it does appear probable that deflection of the falx is related to the appearance of symptoms of raised pressure.

There were seventeen growths beneath the tentorium in my own series. In five of the six examples of cerebellar neoplasm, the signs of intracranial pressure appeared early and were profound. In the one patient without symptoms, who died under an anæsthetic while undergoing the operation of gastro-enterostomy, there had at no time been any suspicion of intracranial mischief. At the post-mortem examination two nodules, each about the size of a cherry, were found in the white matter of the right lobe of the cerebellum, and one about twice the size of the others projected from the under surface of the left cerebellar lobe. Histologically these tumours were all gliomata. It is difficult to understand why this patient failed to suffer from any rise of intracranial pressure—it may be that the tumours being symmetrically situated failed to displace the brain-stem, or occupying a very inferior position in the posterior fossa a certain amount of compensation could occur and the tentorium not be elevated. The condition of the ventricles in the other five cases is of considerable interest. In two of them considerable dilatation of the ventricles is reported, associated with excess of fluid in the sub-arachnoid space; in fact, at the decompression operation on one of these patients, the surgeon stated that about 5 oz. of fluid escaped on incising the dura. In a third case there was moderate distension of the ventricles without any excess of external fluid. In the other two, no obvious dilatation of the ventricles was noted post mortem: the condition of the ventricles seems to suggest that it is very unlikely there was any obstruction to the normal circulation of cerebro-spinal fluid in at least four of the five cases. In the post-mortem records of the two patients with tumours in the cerebello-pontine angle, both of whom suffered from manifestations of raised pressure for a considerable period before death, no mention is made of any displacement of the pons.

although this seems to be the situation where such a condition is most likely to arise. In one where the symptoms had been present for years and secondary optic atrophy had supervened, the lateral and third ventricles are described as being dilated to a fairly great degree, while in the other patient who had suffered from headache, vomiting and double papilloedema for at least five months, there was only moderate distension of the lateral ventricles. It would appear reasonable to anticipate more distension in this time, if any serious obstruction in the region of the aqueduct were present. Experimentally, very pronounced dilatation is known to occur in two to three weeks, but in such cases of course the obstruction is complete. The post-mortem records in neither case of angle tumour refer to any sign of obstruction, but this does not exclude its presence during life.

Of the four patients suffering from tumour of the medulla, two exhibited symptoms of raised intracranial pressure and two did not. In both the former there was obvious obstruction by the growth itself in the region of the fourth ventricle, and a consequent internal hydrocephalus was present. In the two patients without symptoms of increased pressure, one had a small "button-shaped" tumour growing from the posterior aspect of the lower end of the medulla, and in the other the growth involved the whole medulla and caused a general enlargement. From the post-mortem reports it seems possible that compensation for the increased amount of tissue in the posterior fossa might have been made by downward displacement, and this is supported, in the former case at least, by clinical evidence of tension upon the hypoglossal nerve. Any compensation by downward displacement would prevent elevation of the tentorium, and would also render lateral displacement of the brain-stem less likely to occur.

The five remaining subtentorial tumours were all situated in the pons, and in two there appears to have been no definite clinical evidence of increased pressure. In both of these the neoplasm was in the basal part, a situation most remote from the aqueduct, and where some considerable enlargement could occur without elevating the tentorium. In one of these cases it was observed at the post-mortem examination that there was an increase in the amount of fluid in the subarachnoid space; there is no clinical record of the symptoms and condition of the patient immediately preceding death, and this is particularly unfortunate as it seems possible that a raised intracranial pressure was the terminal condition. In all the three cases of pontine tumour in which symptoms of increased pressure were manifested, there was very marked

or extreme dilatation of the lateral ventricles, and in two there seems to be definite evidence of obstruction of the aqueduct; by occlusion from tumour growth in one case, and direct compression of the canal in the other. In the third, there is no record of any obstruction, but it is stated that the neoplasm was growing from the upper part of the pons and projected upwards into the transverse fissure. The two veins of Galen fuse in this fissure to form the great vein of Galen, and it is probable that the extension of the tumour would impede the venous drainage from the choroid plexuses by direct compression.

From an analysis of the seventeen cases of subtentorial tumour there does not appear to be any conclusive evidence of obstruction in the brain-stem except by the growth itself, as in two of the pontine tumours and the two medullary growths which filled the cavity of the fourth ventricle. There seems to be a complete absence of any evidence of obstruction of the aqueduct by displacement of the brain-stem except perhaps in one case of tumour in the cerebello-pontine angle, which is undoubtedly the site that is known to give rise to deflection or torsion of the brain-stem most frequently. Combined ventricular and lumbar punctures in the case of infratentorial tumours do very frequently demonstrate block. In a recent series of twenty-four, Hodgson [6] found it present in two-thirds of them. It is important to remember, however, that this does not necessarily prove the existence of block of the aqueduct, as it may quite probably be located in the region of the foramen magnum and produced by a pressure cone.

DISCUSSION.

From the study of fifty-nine cases of intracranial tumour and the anatomical and physiological considerations of the cranial contents, it is now possible to make certain deductions.

With supratentorial tumours, lateral displacement or torsion of the brain-stem sufficient to produce obstruction of the aqueduct, must be a rare occurrence, and there is some difficulty in believing that it can ever be caused by growths in this part of the cranium. Downward displacement of the brain-stem seems more likely in the case of some supratentorial tumours, but such alteration in position would, on anatomical grounds, tend to diminish the calibre of the great vein of Galen rather than to reduce the diameter of the aqueduct of Sylvius. Furthermore, any displacement of the brain-stem is least possible in tumours situated in the hinder part of the parietal or in the occipital lobes, and yet all records show that symptoms of raised pressure are

much more frequent in the case of growths in these positions than in any other part of the supratentorial division of the cranial cavity. A neoplasm of fair size in the posterior part of the cerebrum is more liable to cause lateral deflection of the falx and consequent elevation of the tentorium than one in the frontal, fronto-parietal, or parietal regions. Therefore, in supratentorial tumours it seems probable that deflection of the falx is a more important factor than displacement or torsion of the midbrain in the production of raised intracranial pressure. It has been shown how elevation of the tentorium can lead to obstruction of the venous drainage from the choroid plexuses, and to excessive production of cerebro-spinal fluid. Therefore I maintain that there is distinctly more evidence in favour of compression of the great vein of Galen as being the cause of pressure symptoms in supratentorial growths rather than any displacement of the brain-stem. Supporters of the latter theory for explaining the symptoms of raised pressure have commonly experienced a difficulty in adapting it to all tumours above the tentorium.

Brain, in a paper to which I have previously referred, after stating that the papilloedema in cases of subtentorial growths and tumours of the ventricles, midbrain and occipital lobes, is due to the rise of intracranial pressure consequent upon obstructive hydrocephalus, goes on to say that "in the case of tumours of the frontal, parietal and temporal lobes it is caused by the local rise of intracranial pressure produced by the tumour itself." He thus divides the cases into two groups: the first group (tumours of the third and fourth ventricles, cerebellum and the one case of occipital tumour in his series) in which hydrocephalus is caused early by obstruction; and the second group (tumours of the frontal, parietal and temporo-sphenoidal lobes), in which hydrocephalus is absent or occurs later. He obtains this subdivision by reference to the relative time of onset of the vomiting, which does undoubtedly appear to be the earliest and most important sign of dilatation of the ventricles and of papilloedema. In the first group, he believes vomiting occurs very early, is one of the first symptoms to be complained of, and precedes the onset of papilloedema. In the second group, he maintains the papilloedema precedes vomiting, since there is usually "a rise in pressure within the optic sheaths before the occurrence of obstruction of the aqueduct of Sylvius." Brain does not submit any records in support of this subdivision, so it may be helpful to analyse the clinical histories of the 59 cases referred to in this paper, on these points.

It was disappointing to find that in only 16 cases (six in Group I

and ten in Group II) were accurate records available of the time of onset of vomiting and papilloedema, but in spite of this small number the information is of some value. In the six cases in Group I, vomiting preceded the papilloedema in five, and succeeded it in only one case; in two of the former, the fourth ventricle was obstructed by the growth. Of the ten cases in Group II, papilloedema preceded vomiting in four, and the latter was the earlier symptom in six. These cases do not lend very definite clinical support to the division suggested by Brain, but, excluding for the moment cases of obvious obstruction to the cerebro-spinal fluid path by tumour, they do seem to indicate that tumours in sites which predispose to the early occurrence of symptoms of intracranial pressure are most likely to cause early dilatation of the ventricles. Such an indication is not necessarily in favour of obstructive hydrocephalus as the cause of the increased pressure, since the early dilatation of the ventricles may be brought about by excessive production of cerebro-spinal fluid as well as by interference with its outflow from the ventricles.

As Brain has pointed out hydrocephalus may be produced in these cases in at least two ways: first, by an absolute obstruction of the aqueduct or fourth ventricle; and secondly, by excessive production of cerebro-spinal fluid, causing a relative obstruction, as the aqueduct would be too narrow to provide for the escape of the fluid at the same rate as its production. Occipital tumours and subtentorial tumours cause symptoms of raised intracranial pressure earlier and more frequently than frontal, fronto-parietal and parietal tumours, and these figures seem to indicate that when the symptoms occur hydrocephalus tends to supervene sooner in the former than in the latter. The figures only indicate a tendency and do not appear to me to justify a division into two groups, or to be sufficiently reliable to place much confidence with regard to site upon the relative time of the onset of papilloedema and vomiting. They do not support the belief that all cases of occipital and subtentorial growths give rise to an obstructive hydrocephalus. When we refer back to the post-mortem findings in the examples of cerebellar tumour, it will be remembered that it appeared very unlikely that in four out of the five cases manifesting raised intracranial pressure was there any obstruction to the normal circulation of cerebro-spinal fluid. This must cause us to hesitate to believe that the tendency to early dilatation of the ventricles in many subtentorial growths is an indication of obstruction by displacement of the brain-stem or similar means. My records show that hydrocephalus does occur quite frequently

in these cases without any obstruction being present. Consequently it seems safe to presume that in a large proportion the ventricular dilatation must be due to such an increased production of fluid and that it cannot escape sufficiently quickly through the narrow aqueduct. As far as I can determine, such excessive production can only be induced by impaired venous drainage from the choroid plexuses by the great vein of Galen, which vessel could be compressed by elevation of the tentorium. Neurological literature contains numerous records of cases of subtentorial growths which exhibit no narrowing of the aqueduct, even at the time of the post-mortem. As an example, the report of a case of cerebellar tumour by Rhein [10] may be quoted. It was recorded in order to illustrate the supervention of hypophysial symptoms from great distension of the third ventricle; both lateral ventricles were "enormously" distended, the third being 2 cm. in diameter and 2.5 cm. in depth, whilst the fourth was also "much distended," which must exclude any obstruction in the aqueduct by displacement or other cause. The tumour was situated in the right cerebellar hemisphere, which was about one-fourth larger than the left, and it is of interest to notice that the photographs of the brain on section show that the right lateral ventricle is less dilated than the left, which is quite possibly due to greater elevation of the tentorium on the affected side.

From this consideration of tumours below the tentorium, it seems probable that excessive production of cerebro-spinal fluid, rather than displacement and torsion of the brain-stem with consequent obstruction, is the more important factor in the production of increased intracranial pressure in subtentorial as well as supratentorial tumours. Some subtentorial tumours block the fourth ventricle, as two of the medullary growths previously referred to, and some in the cerebello-pontine angle cause such displacement of the brain-stem that obstruction to the aqueduct is possible, but excluding these it is clear that evidence of excessive production of fluid is a much commoner post-mortem finding than an obstructive hydrocephalus.

Further reference to pontine tumours is necessary. The pons lies below the hiatus tentorii rather than below the tentorium, and consequently considerable enlargement of this part of the brain-stem is possible without elevation of the tentorium. It is of interest to notice that tumours in this situation, provided they do not extend under the tentorium, may exist for long periods without giving rise to symptoms of raised intracranial pressure. My records suggest that in those cases where an increased pressure existed without extension under the

tentorium, there is evidence of obstruction of the aqueduct by direct pressure of the tumour upon or into the aqueduct, leading to marked dilatation of the ventricles. It seems likely that pontine tumours may thus cause pressure symptoms either by compressing the aqueduct and causing an internal hydrocephalus, or by extension under the tentorium, leading to elevation of this structure and consequent excessive production of fluid by interfering with the venous drainage from the choroid plexuses.

There were no examples of pineal tumour in my series, but it is highly important to consider them, as from their situation it is conceivable that they might obstruct the aqueduct by pressure downwards, or compress the great vein of Galen by extension in an upward direction. For the further discussion of these two possibilities I shall refer to the recent valuable contributions to our knowledge of pineal tumours by Horrax and Bailey. In the paper by Horrax [7] on the differential diagnosis between pineal and pontine tumours, the following important point is stressed—"the initial symptoms in all the pineal group were due to increased intracranial tension." He found that all the fifteen patients with primary pineal growths first complained of pressure symptoms, whereas only six patients out of fifteen with primary pontine tumours suffered initially from the manifestations of increased intracranial tension.

It is quite evident from the clinical records that in pineal cases the raised pressure occurs at a very early date, whatever the cause may be. The difference in time of onset of the pressure symptoms in the two groups is alleged to be due to the fact that even small pineal growths tend to block the aqueduct. It can be understood anatomically how a mass in the region of the pineal gland can press down upon the dorsal surface of the midbrain, and lead subsequently to partial or complete obliteration of the aqueduct, but it seems reasonable to suppose that pressure sufficient to induce this would be most likely to cause clinical symptoms from compression of the quadrigeminal bodies at least simultaneously with, if not before, those due to the blocking of the aqueduct. Furthermore, it must be remembered that any slight enlargement of the pineal in an upward direction must inevitably compress the great vein of Galen against the splenium. Anatomically, compression of the vein seems more likely at an early date than obstruction of the aqueduct, and without at least the simultaneous appearance of signs of involvement of the quadrigeminal bodies with the pressure symptoms, it would be rather unwise to suggest that the late reduction in size

of the lumen of the aqueduct. When we turn to the details of the extent of twelve of the pineal tumours presented in the paper by Horrax and Bailey [8], considerable light is shed on the problem. Although the condition of the ventricular system is not recorded in every case, it is possible to conclude from the information given and the illustrations presented that in some cases there was no obstruction of the aqueduct even at the time of death. In Case 4 it is recorded that *all* the ventricles were greatly distended; in Case 11 the aqueduct is described as patent, and the fourth ventricle can be seen to be distended in the photograph. In Case 6 it is stated that there was marked dilatation of *the* ventricles, which presumably refers to all. The illustration of the brain in Case 2 seems to show some distension of the fourth ventricle, and also in Case 8, although in the latter some compression of the aqueduct is also evident. The photographs of the brain in Cases 8 and 12 suggest definitely that the aqueduct was patent, although small in Case 12. In Case 7 the aqueduct was obliterated, and could not be identified at the post-mortem examination. Although there is no evidence one way or the other in several instances, it seems * probable that there was no very serious obstruction of the aqueduct in seven, and in three—possibly four—it is clear that there was no obstruction even at the time of death. In some of the reports it is noted, and perfectly demonstrated by the illustrations, that the splenium of the corpus callosum was pushed upwards and flattened, and the normal distance between the splenium and the brain-stem appreciably increased in consequence. Such upward pressure and displacement by a pineal growth must necessarily compress the great vein of Galen against the splenium. The absence of any evidence of compression of the aqueduct, even as a terminal condition, in some of these cases makes it certain that obstruction at this point cannot invariably be the cause of the symptoms of raised pressure in all instances of growth of the pineal gland. One is led to wonder whether it is ever the initial cause when noting that in Case 11 the aqueduct was found to be patent at post-mortem examination, although pressure symptoms had been present for seven months. In the face of this, of our knowledge of the position of the great vein of Galen, and of the fact that the splenium is often displaced upwards and flattened by pineal growths, it seems reasonable to conclude that in at least a proportion of these cases interference with the venous drainage is the primary cause of the raised intracranial pressure.

At post-mortem examination marked dilatation of the lateral and third ventricles is seen, and is due by such relatively slight distension

of the fourth ventricle that it may pass unnoticed, or no attention is paid to it. Such a condition is liable to be interpreted as demonstrating obstruction in the region of the midbrain. Without there being any obstruction, it is common to find the fourth ventricle relatively less dilated than the lateral. In a specimen of tumour in the parietal region recently examined I found the lateral and third ventricles enormously distended and out of proportion to the distension of the fourth ventricle, although the aqueduct was not only patent but showed some dilatation. There appear to be obvious reasons for this; in the lateral and third ventricles the production of fluid by the choroid plexuses is so great that only a proportion of it can be drained off along the aqueduct, consequently the pressure in these cavities rapidly rises and dilatation results.

It has been already noted—and it is necessary to repeat—that proof has been advanced of cerebro-spinal fluid being still produced when the ventricular pressure is considerably raised above the normal. In the case of the fourth ventricle, the production of fluid in the chamber by the small choroid plexuses in this region cannot be very great, and the pressure will depend largely upon inflow by the aqueduct, and outflow into the subarachnoid space by the foramina of Majendie and Luschka. Until the aqueduct is dilated very considerably, it seems unlikely that the inflow will greatly exceed the outflow, and consequently it is reasonable to suppose that the fourth ventricle will usually not dilate so rapidly or to the same degree as the lateral and third ventricles. It is possible that some large tumours in the posterior fossa may impede the drainage of the fluid through the foramina in the roof of the fourth ventricle. Such a condition, when it arises, would clearly cause a greater rise of pressure in the fourth ventricle and greater dilatation of its cavity. The condition of the fourth ventricle has been alluded to in some detail, as the absence of any obvious distension of this chamber, in cases where the lateral and third ventricles have exhibited definite dilatation, has been used as evidence of primary obstruction in the region of the aqueduct. I suggest that marked differences in the extent of the distension of these cavities can occur without any obstruction.

It seems possible that in the late stages an internal hydrocephalus, whether produced by an excessive amount of cerebro-spinal fluid or by an obstruction, can interfere with the absorption of the fluid and so increase the already raised intracranial pressure. Great dilatation of the ventricles compresses the cerebral tissue against the membranes and the bones of the skull, as is manifested by the flattening of the con-

volution usually observed with a high degree of internal hydrocephalus. Such compression against the rigid walls must obstruct the normal ascent of the fluid over the hemispheres towards the superior longitudinal sinus, and so diminish absorption of the fluid which is already present in an excessive amount. This interference with absorption is clearly secondary to the hydrocephalus, and will only increase further the already raised intracranial pressure and not be the original cause of it. The accumulations of fluid at the base, particularly in the posterior fossa, which are reported in some operation and post-mortem records, may be due to this cause.

CONCLUSIONS.

(1) Evidence is submitted to show that there is very rarely any primary obstruction of the aqueduct in cases of supratentorial tumour. When it does occur, it is probably always due to direct pressure upon the aqueduct by the growth, as in some examples of pinealoma, or occlusion by the neoplasm itself. There seems to be good reason for believing that the raised intracranial pressure associated with tumours above the tentorium is originally caused by deflection of the falx, and consequent compression of the great vein of Galen, which induces an excessive production of cerebro-spinal fluid.

(2) Tumours below the tentorium may more readily obstruct the outflow of cerebro-spinal fluid from the ventricular system, but in a proportion no block is present. In the latter, at least, it seems likely that the cause of the raised intracranial pressure is due to elevation of the tentorium with consequent compression of the great vein of Galen.

(3) It seems likely that raised intracranial pressure associated with tumours within the cranium is more commonly due to compression of the great vein of Galen than to any other cause.

(4) Whilst obstruction to the venous drainage from the choroid plexuses or block in the region of the aqueduct or fourth ventricle, separately or in association, probably explain the *origin* of the raised intracranial tension, it must be mentioned that there are a number of other factors to be considered. It would appear, however, that these factors are of secondary importance and lead merely to an increase of the already raised pressure.

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THE ELECTROMYOGRAM IN MYASTHENIA GRAVIS.

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THE electromyogram, by quantitatively recording the electrical currents associated with muscle contraction, is often an aid in understanding the nature of unusual or abnormal contractions. From the rhythm, frequency and height of these action currents taken when the muscle is fresh and when exhausted, the site of disease causing impaired muscle function can sometimes be defined.

Since myasthenia gravis was first described by Wilkes, in 1877, and more fully by Erb, in 1878, many theories as to its causation have been advanced [1], [2], [3], [9]. As yet none can be accepted.

It may be inferred from histopathological observations [2], [3], [4], [5] that, in addition to any possible disturbance in innervation, the muscle structure itself is altered so that normal or complete contractions would be extremely improbable. The studies of the muscle physiology [4], [6], [7], [8], [9] in myasthenia gravis further indicate that the main defect in function lies peripheral to the anterior horn cell. Furthermore, because of the characteristic appearance of the action currents during normal fatigue, it should be possible to discover whether the exhaustion of myasthenia is brought about by "excessive fatigability," as is often inferred, or by failure of contraction for other reasons.

The first attempt to study the action currents of muscle in myasthenia gravis was made by Marinesco and Athanasiu [10]. A Brocas' galvanometer was used and action currents qualitatively similar to the normal were obtained. The intensity of these currents was, however, five to six times more feeble.

The electromyographic record of the intact human muscles during exercise presents two types of waves [11]: (1) Large primary waves (Hauptwellen), to which most of the studies have been confined; and (2)

numerous smaller waves (Nebenzacken) superimposed on the larger waves. Richter [12] recognizes still a third type of wave of very small amplitude which he calls secondary waves, and which he concludes are due to impulses from higher centres.

The frequency of the primary waves during the contraction of the normal unfatigued muscle ranges from 40 to 60 per second (see Tables III to IV). As exercise is continued to the point of fatigue, the frequency of the waves decreases to as low as 25 to 30 per second, and the amplitude of the primary waves increases [13].

Herzog [14] recorded the action currents set up in the flexors of the fore-arm of a myasthenic patient when a dynamometer was pressed. He found that although exhaustion set in rapidly, the frequency of the action currents did not decrease but remained constant. The amplitude of the waves at the beginning of the work was much smaller than in the normal person and, as fatigue set in, the amplitude diminished.

Schäffer and Brieger [15] recorded the action currents of the left trapezius in a case of myasthenia gravis while the patient supported a weight of 0.5 kg. Their results were the same as those of Herzog. The frequency of the waves did not change but their amplitude became smaller. They also repeated and confirmed the other experiments of Herzog.

Our patient had the following history and physical abnormalities:—

Case.—A. G., a 30-year-old white man, was admitted to the Boston City Hospital in July, 1927.

Previous to the age of 27 he considered himself perfectly well. Two years before admission (1925) he noticed that he fatigued easily, and "was very nervous," perspired freely, had diplopia, and weakness of the wrist muscles. Nervousness, fatigability, sweating, palpitation, dyspnoea, irritability and insomnia increased steadily until the patient came to the Lahey Clinic (Boston) on April 27, 1926.

Physical examination revealed an enlarged thyroid, exophthalmus, widened palpebral angles, tremor of hands and feet, a heart-rate of 120, and a blood-pressure of 100. He had lost almost 50 lbs.

A diagnosis of primary myasthenia gravis was made, and he was admitted to

was unable to phonate clearly. When reaching for an object he seemed unable to extend his arm completely.

On re-examination at this time his skin was pale and pasty, loss of hair and the exophthalmus persisted. The pulse-rate was 70. He had very little strength and was exhausted readily.

His basal metabolic rate was found to be minus 18 per cent. Thyroxin was administered and the metabolism approached normal. X-ray plates showed no enlargement of the thymus gland.

In May, 1927 (about nine months later), he had paralysis of the superior recti muscles of the eyes, and marked exophthalmus. His basal metabolic rate was plus 27 per cent. In June he was discharged somewhat improved. He entered the Boston City Hospital for study a month later. At the time of entrance he was extremely weak and exhaustion was caused by merely sitting up for a few minutes.

In our experiments the action currents of the myasthenic muscle during voluntary contraction to exhaustion were compared with those of normal muscle under the same conditions.

Because of Marinesco's [2] interesting observation that the myasthenic reaction could be produced in the normal by hyperæmia or ischæmia, these conditions were experimentally reproduced on a normal person and the result compared with the myasthenic.

A patient with progressive muscular atrophy¹ was studied with the myasthenic. It was thought that comparison with a syndrome known to be caused by degeneration of the ventral horn cells might be of interest.

METHOD.

The method used was a slight modification of that described by Cobb and Forbes [13]. The right arm was fixed in an apparatus which held the fore-arm horizontally by means of a series of leather straps. The upper arm was also fixed by means of straps to a board flexed at an angle of 120°. No motion of the elbow was possible. The hand was inserted into a plaster of Paris glove, so that motion of the wrist-joint only was possible. A wire was attached to the plaster glove and connected with a pair of springs attached to an upright board. Between these springs a fine wire was stretched. The shadow of

dynamometer springs, and the wire which was stretched between them cast a shadow that fell on the film and made a tracing along with the electromyographic record. The pull on the springs was calibrated, so that the work done could be approximately gauged.

The Hindle galvanometer in the regular electrocardiograph station

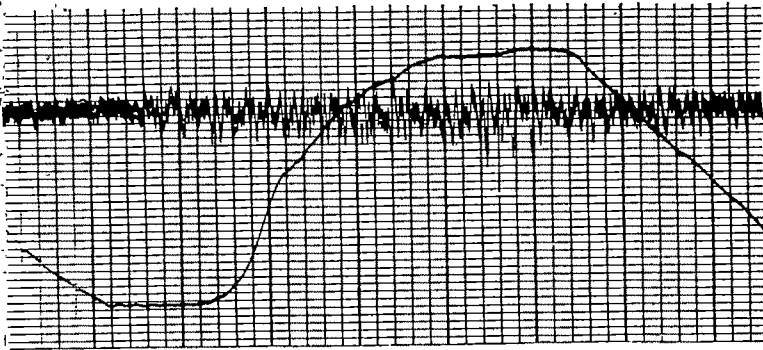


FIG. 1.—Electromyogram of normal subject (H. G. W.) (sixth contraction). The muscle contraction against the pull of the spring is recorded by the upstroke of the mechanogram¹. The larger action currents begin before the onset of the pull, are obvious at the height and disappear with relaxation. The pull at the height of contraction is 5 kg.

¹ In all records the ventricular lines mark periods of $\frac{1}{75}$ second.



FIG. 2.—Electromyogram of patient with myasthenia gravis (sixth contraction). The record on the action currents shows less obvious difference between contraction and relaxation. The pull at height of contraction is 266 grm.

was used. The string was adjusted to such a tension that a difference of potential of 1 millivolt would cause a deflection of 1 cm. The electrodes consisted of small zinc plates about 2 cm. in diameter, soldered to binding posts which received the wires connecting with the

instrument. The skin was thoroughly cleansed and the electrodes applied, with thick pads of cotton-wool soaked in salt solution between them and the skin. They were firmly held in place by means of wide strips of adhesive plaster. One electrode was placed over the flexors of the fore-arm and the other, the "indifferent electrode," over the skin of the lateral surface of the arm just below the insertion of the deltoid muscle.

Electromyograms on patients and normal controls were obtained one after the other without changing the apparatus. The subject flexed the wrist against the resistance of the ergograph until extreme fatigue occurred, and during this time the electrical responses were recorded beside the curves representing the mechanical work. In the case of the patients it was practical to photograph the entire course of the exercise, because of its comparatively short duration. With the normal controls this was impracticable, but periodic exposures of several minutes' duration were made.

TABLE I.

Subject—A. G., myasthenia gravis.

Number of contractions		Frequency of primary waves		Amplitude in mm
1	..	40	..	3.4
2	..	45	..	3.5
3	..	35-45	..	3.5
4	..	35-40	..	3.5
8	..	35-40	..	3.5
9	..	35-40	..	2.5
11	..	35-40	..	3.6
Sustained contractions of 10 seconds				
Beginning	..	40-45	..	4.5
End	..	40	..	3.4
13	..	40	..	3.1

TABLE II

Subject—A. G., myasthenia gravis

Number of contractions		Frequency of primary waves		Amplitude in mm
1	..	35-40	..	4.6
2	..	35-40	..	3.6
3	..	35-40	..	3.6
5	..	35-40	..	3.6
6	..	40	..	3.4
9	..	35-40	..	3.6
Sustained contractions of 8 seconds				
Beginning	..	40	..	3.6
End	..	40-45	..	3.5

The frequency and amplitude of the primary waves was measured from the prints of the films. The personal equation is here significant, for the "Nebenzacken" are very confusing. Furthermore, the rhythm of action currents during contraction is subject to variation, the more powerful contractions showing more regular rhythm than

weaker ones. Therefore, minor differences were waived and attention directed to the more significant alterations. Because of these possible sources of error, the frequencies given in the tables represent the possible maxima and minima which could be derived from the same films by different observers.

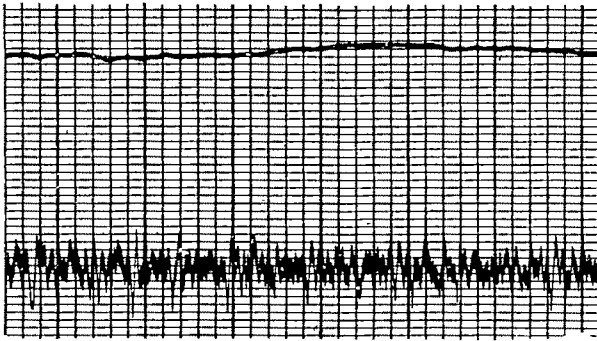


FIG. 3.—Electromyogram of normal subject. Beginning of sustained contraction. Note reduction in frequency and definite increase in amplitude.

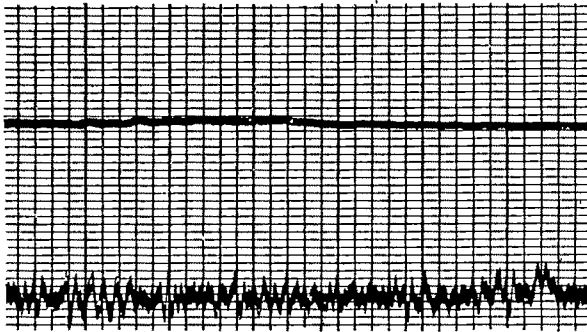


FIG. 4.—Electromyogram of patient with myasthenia gravis. Beginning of sustained contraction. Note slight reduction in frequency and slight increase in amplitude.

OBSERVATIONS.

The myasthenia patient was rapidly exhausted by the pull against the ergograph. At the height of contraction the pull was 266 grm. In Experiment 1 eleven short contractions were made, then a sustained contraction of ten seconds, after which only one more very feeble contraction, barely perceptible on the mechanogram, was possible. After recovery the experiment was repeated. This time only nine short contractions, lasting one to two seconds each, and one prolonged contraction of ten seconds, were possible.

The results of these experiments are recorded in Tables I and II, and portions of the records are represented in figures 2, 4 and 6.

At the beginning of the first experiment the frequency of the primary waves was 40 to 45 per second, and at the end it was practically the same. The amplitude at the beginning was 3 to 4 mm., and without appreciable change at end. In the second experiment the results were practically the same (see Table II).

The normal control done immediately afterwards is recorded in Table III.

TABLE III.

Subject—H. G. W, normal male.

Number of contractions		Frequency of primary waves		Amplitude in mm
1	..	45-50	..	4-9
2	..	50	..	6-10
3	..	50	..	6-10
4	..	45-50	..	6-12
10	..	35-40	.	—
15	..	50	..	—
21	..	30-40	..	8-14
22	.	30-40	..	8-14
23	..	30-35	..	10-17

At the height of contraction the pull was 5 kg. Here there was a frequency of 45 to 50 per second at the beginning in each case, with a decrease to 30 or 35 at the end. The amplitude increased considerably as fatigue set in.

In Table IV are the results of one experiment on a normal subject, H. G. W., during a period of local hyperæmia. A blood-pressure cuff was

TABLE IV.

Subject—H. G. W., normal

Condition—Blood-pressure cuff around upper arm and inflated so as to stop venous blood-flow.

Number of contraction		Frequency of primary waves		Amplitude in mm.
1	..	50-55	..	4-7
2	..	50-60	..	4-7
3	..	50-60	..	4-7
5	..	55-60	..	5-9
7	..	45-50	..	4-9
(Work continued without recording)				
1	..	50-60	..	4-10
2	..	50	..	4-9
3	..	45-50	..	5-11
4	..	45-50	..	5-11
5	..	40-45	..	5-12
6	..	40-45	..	4-11
7	..	40-50	..	5-10
(Work continued without recording.)				
1	..	45	..	5-7
2	..	40-50	..	5-10
3	.	40-50	..	5-10
5	..	40-45	..	5-9

placed about the upper arm of the subject just below the axilla. To produce the desired stasis the cuff was pumped to just below the arterial pressure. Electromyograms were then taken during exercise to fatigue. It was found that at the beginning of work the frequency of the primary waves ranged from 45 to 50 per second, and the amplitude was

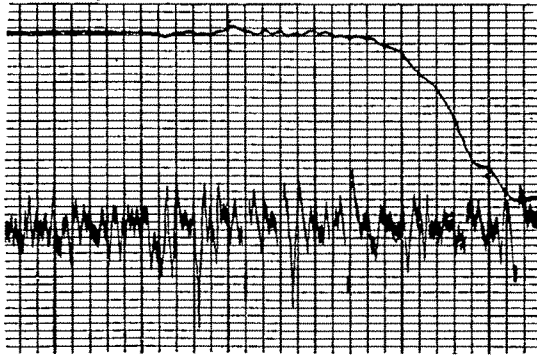


FIG 5.—Electromyogram of normal subject. End of sustained contraction
Note reduced frequency and great amplitude.

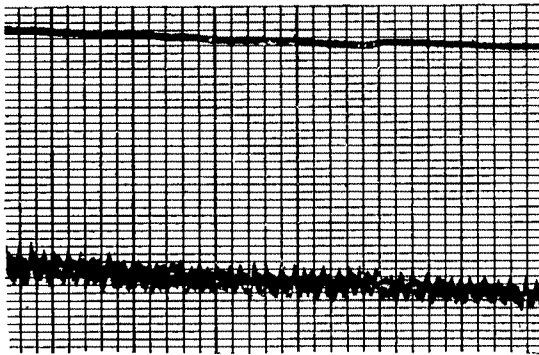


FIG 6.—Electromyogram of subject with myasthenia gravis. End of sustained contraction.
Frequency and amplitude practically constant and unchanged.

4 to 8 mm. At the end of the experiment, after extreme fatigue had set in, the frequency of the primary waves was 25 to 30 and the amplitude 6 to 12 mm.

After sufficient rest the experiment was repeated. Contractions were now begun again, and continued to fatigue and practically to

exhaustion (Table IV). This time the frequency of primary waves at the beginning of the experiment was 50 to 60 per second, with an amplitude ranging from 4 to 7 mm., while toward the end, when extreme fatigue was evident, the number of primary waves was 40 to 50 per second and the amplitude 5 to 10 mm.

After another recovery period the experiment was repeated without inflation of the blood-pressure cuff. The frequency of the waves was 50 to 60 per second at the beginning of the contractions and 30 to 40 per second at the end. The amplitude was 5 to 8 mm. in the beginning and 5 to 11 mm. at the end.

The patient with progressive muscular atrophy was examined in the same way as the myasthenic patient. One electrode was placed over one of the atrophied muscles, the flexor carpi radialis, and the other over the outer aspect of the upper arm. The results are recorded in Table V. The frequency at the beginning is from 45 to 60 per second, while at the end it is as low as 25. The amplitude at the beginning of the first experiment is 3 to 10 mm., it then goes up to 5 to 11 mm., and in the final contraction again drops. In the second experiment (Table V) the amplitude is 4 to 8 mm. at the beginning, going up to 4 to 12 mm. towards the end, but again dropping in the last contraction.

TABLE V.

Subject—T. M., progressive muscular atrophy.

Number of contraction	Frequency of primary waves	Amplitude in mm
1	45-60	4-8
2	45-55	4-9
4	50-60	3-7
6	50-55	4-9
10	45-55	5-12
13	45	4-11
16	35-45	4-12
17	35-45	4-12
18	—	—
Lasting 15 seconds.		
Beginning	40	5-9
End	25-40	4-8

COMMENT.

The exact mechanism of the action current in intact muscle during voluntary contraction is not known. There are two reasonable conceptions. One is that each muscle action current is the electrical response on the part of the muscle to a single impulse coming to it from the motor nerve. This implies that the action currents of the nerve

and muscle have the same frequency. Dittler and Garten [16] and Gasser and Newcomer [17] have proven this for the phrenic nerve and diaphragm of animals by taking action currents off both, simultaneously. Since in fatigue the muscle action currents decrease in number, this view would lead one to infer that fatigue sets in at synapses in the cord or higher, thus letting fewer impulses travel down the motor nerve.

The other view is that the number of impulses travelling down the nerve toward the muscle is relatively high, and that the number of the muscular action currents is determined by some factor peripheral to the nerve. Cobb and Forbes [13] put forth the view that the place of adjustment is in the myoneural junction, and that the decrease in frequency during fatigue corroborates this. Their conception of delay at the myoneural junction explains the increase in amplitude of the primary waves with fatigue. The muscle fibres in the latter state cannot contract until later in the relative refractory period, and the amplitude of the response becomes greater. As an alternative to this they consider the seat of fatigue to be in the muscle fibres.

Our results on myasthenic muscle are practically in agreement with those obtained by previous observers. The primary waves of the myasthenic muscle are very small in the beginning, and the frequency of the primary waves remains constant, while in the normal individual it decreases. The amplitude remains practically constant in the myasthenic muscle, with slight increase during the first work, and then later possibly a slight tendency to decrease. Herzog [14] and Schäffer and Brieger [15] found the amplitude to decrease with exhaustion. Certainly there is no increase in amplitude. In normal muscle the amplitude increases conspicuously with fatigue.

The interpretation of these observations is that the exhaustion of myasthenic muscle is different from that of normal muscle. It is possible that the evidence of physiological fatigue could be demonstrated electromyographically if the muscle continued to contract, but that the myasthenic muscle loses its contractibility before the onset of "fatigue."

Our electromyographic records of muscle with venous stasis do not vary enough from the normal to permit us to accept the theory that excessive accumulation of acid metabolites is responsible for the myasthenic syndrome.

The electromyogram of the patient with progressive muscular atrophy differs little from the normal, with the exception of the decrease in amplitude in the final sustained contraction. Since the amplitude of the electromyogram depends, among other things, on the tension [18]

the final decrease in amplitude observed in the records may be the result of a gradual relaxation during the last fifteen to sixteen seconds. That there was relaxation is shown in the mechanical record on the film. Before the final contraction, the increase in amplitude and the decrease in frequency, as in the normal, is definite.

The essentially normal electromyogram of progressive muscular atrophy is in keeping with our conception of its essential difference from myasthenia gravis. In progressive muscular atrophy the primary degeneration is in the ventral horn cells, leading to a reduction in the number of nerve, and secondarily, of muscle units. The electrical responses of the remaining muscle units are those of normal muscle. On the other hand, in myasthenia gravis there may be a change in muscle cells, causing a generally reduced electrical response. If the muscle action be feeble only feeble action currents can result.

CONCLUSIONS.

(1) Electromyographic studies of the action currents of actively contracting muscle in a patient with myasthenia gravis reveal definite abnormalities. The frequency of the primary waves does not change with the onset of exhaustion, nor does the amplitude, which is small from the onset, increase. It usually remains small or may even decrease.

(2) Electromyographically the exhaustion of the muscle in myasthenia gravis is very different from the fatigue of normal muscle. The absence of adequate action currents indicates an absence of adequate muscle action, or contractibility, and not "excessive fatigability."

(3) Electromyographic evidence further indicates that the muscle exhaustion in myasthenia gravis is due to a fundamental defect peripheral to the ventral horn cell, and probably in the muscle cell.

We wish to express our thanks to the Director of the Thorndike Memorial Laboratory, of the Boston City Hospital, for allowing us to use the string-galvanometer, and for giving us the privilege of keeping our patient, A. G., on the Research Ward during the nine-day period of study. We also wish to thank Miss Hayes for technical assistance in the making of the records.

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NOTICES OF RECENT PUBLICATIONS.

Nouveau Traité de Médecine. Fascicule 18: *Pathologie du Système nerveux; Sémiologie générale.* Pp. 812 Paris: Masson et Cie. Price 85 francs. Fascicule 21: *Nerfs; Sympathique; Névroses.* Pp. 900. 1927. Price 85 francs.

Volume xviii of the encyclopædic "System of Medicine," which is appearing under the editorship of Professors Roger, Widai and Teissier, is the first of the four volumes to be devoted to the nervous system. It is designed on a plan favoured by the French in which disturbance of each function, as hemiplegia, ataxia, anomalies of sensation, &c., is dealt with separately, regardless of the clinical conditions with which it is associated and often with little reference to its pathology. It is obvious that this method has certain advantages in a system intended for the general practitioner, but it may also be of considerable service to the specialist who wishes to revise his knowledge.

It is impossible to refer here to all the chapters, each of which has been written by a recognized authority. Some, as those on "Coma and Apoplexy," by Janowski; "Headaches," by Lévy Valensi; and "Disturbances of Sleep," by Logre, are too short, owing probably to exigencies of space, but many chapters give detailed descriptions and satisfactory analyses of the symptoms with which they deal. Logre and Pascal, for instance, describe the commoner mental disorders from a clinical standpoint in about 100 pages, and almost as much space was allotted to the late Charles Foix for his admirable chapter on aphasia. This is modelled largely on Pierre Marie's doctrines and does not take into account much of the recent English and German work, but as a presentation of the subject to the ordinary physician it could scarcely be improved. Foix and Chavany's section on reflex disturbances is equally good. There are also chapters on paraplegia, hemiplegia, ataxia, disturbance of tone, various forms of involuntary movement and convulsions, in which the clinical features of these conditions are chiefly emphasized. Bourguignon writes on *chronaxie*, de Lapersonne and Velter on visual disturbances, Hautant on examination of the ears and vestibular apparatus, and Sicard on the cerebro-spinal fluid.

Volume xxi deals with various nervous disorders in a more systematic manner. Nearly half its pages are occupied by a series of chapters, all written by Tinel, on traumatic and other affections of the peripheral nerves and roots, multiple neuritis and neuralgia; these all attain the high level that might be expected from the pen of this author. Short sections on vasomotor and sympathetic affections follow, and an interesting chapter by Heuyer on trophic

disturbances, in which in addition to common affections, as bedsores, perforating ulcers and von Recklinghausen's disease, rarer conditions, as angioneurotic and trophic oedema, lipodystrophia and facial hemiatrophy, are fully described. Christiansen writes well on migraine, and Klippel and Weil on epilepsy. Among other subjects dealt with are the common psychoneuroses, the choreas, tics and tetany, and the volume ends with an article by Crouzon on familial diseases of the nervous system. The authority and experience of the authors, the clear and logical manner in which they present their subjects, and the broad clinical attitude most of them adopt make the volume useful both as a textbook and a work of reference.

Die chirurgische Behandlung der Gehirntumoren. Von H. OLIVECRONA.
S. 344. Berlin: J. Springer. 1928. Price M. 27.

This long monograph on the surgical treatment of cerebral tumours is based on the author's personal experience of only 105 cases, in 88 of which the diagnosis and localization were verified. The relatively small number of cases and the short descriptions of the clinical symptoms presented limit the value of the work, though it is instructive to study the experiences of one observer. Unfortunately the question of diagnosis by clinical methods is treated very cursorily and the principles of localization are scarcely referred to, yet the author insists that the surgeon should be his own neurologist. The large proportion of cases in which the tumour was not found is therefore not surprising, and the results are correspondingly disappointing: for instance, only five of twenty-eight patients with supratentorial gliomata survived any time.

He devotes separate chapters to the gliomata, meningiomas, acoustic tumours, &c., and gives records of all the cases of each group he observed. In conjunction with Lysholm, who has furnished some remarkably good radiograms, he discusses radiological diagnosis, ventriculography, puncture of the brain and ventricular puncture as aids in localization. The methods of surgical treatment presented offer little new, but it is of interest that he favours simple decompression in certain gliomata, and insists on the value of two or even three stages in many operations.

Die Tumoren des Gehirns, ihre Symptomatologie, Diagnostik und operative Behandlung. Von L. PUUSEPP. 1te und 2te Lieferung.
S. 444. Tartu-Dorpat: J. G. Krüger. Price 4 dollars.

The author, who was a pupil of Bechterew and later became a "surgical neurologist," has written a very interesting contribution to the Diagnosis and Treatment of Tumours of the Brain, based on his own experience of over 500 cases. In the two parts under review he deals with supratentorial growths, and will, in the third section which has not yet been published, treat of tumours of the posterior fossa, as well as the pathology, symptomatology and principles of surgical treatment. After a short chapter on operative

technique, in which he states that he first employed general anæsthesia then local, but reverted to ether as he has found that local anæsthesia has few advantages and many disadvantages, he discusses the so-called pseudotumours and describes his own findings in the cases of this condition he has met. A short and unconvincing account of symptoms of cerebral tumour in epidemic encephalitis follows. He then passes on to deal in separate chapters with tumours of different parts of the brain, as of the frontal, central, parietal and temporal lobes, of the basal ganglia, the hypothalamic region and of the pituitary. In each section he discusses first the chief symptoms and signs on which a diagnosis can be based; then describes illustrative cases and the nature of the tumours he examined; analyses the localizing signs which his cases presented, and points out the frequency and value of each. He finally deals with the problems that confront the surgeon in the treatment and the results of his own operations. The clinical records which he publishes are adequate and make interesting reading, and his discussions on both the clinical and the surgical aspects of the subject full and instructive, but the histology of the tumours is neither up to date nor satisfactory, and many of the illustrations are poor.

Introduction biologique à l'Étude de la Neurologie et de la Psychopathologie. Par C. v. MONAKOW et R. MOURGUE. Pp. 416. Paris: Félix Alcan. 1928.

This important work presents Professor von Monakow's biological conception of the nervous system as the integrating agent for all the vital tendencies. and whether the biological principles he formulates appear entirely valid or not, they are certainly stimulating and congruent. Much of the material will be familiar to those acquainted with the writings of von Monakow and his pupils; but it has not previously been collected together as a body of doctrine, covering the disordered as well as the normal activities of the nervous system.

The more speculative portions are open to many objections, the mention of "diaschisis" and of its newly-coined counterpart "diaspasis" (denoting the mode of disintegration of function in the instinctual sphere) will sufficiently recall the criticisms that may be made of some of the notions of the Zürich school. It would be impossible to summarize, much less to examine, the original views here so lucidly presented. In many parts of the book, especially those dealing with development, the senior author speaks with magistral authority.

No countenance is given to such divisions as into mental and physical, functional and organic, physiogenic and psychogenic, nor to the sundering of embryology, anatomy, psychology, clinical investigation, pathology; the findings of these various systems are correlated with great ingenuity. The treatment is at times semi-philosophical, neologisms abound and at least one metaphysical notion, that of the *Horme*, the propulsive tendency of the living being towards a creative adaptation of life, is introduced; time and value are stressed as most

important factors in the integration and disintegration of function. At the same time details of development and minute structure are given their due place in the scheme and illustrated by photographs of specimens in the unrivalled collection at the Institute of Cerebral Anatomy.

The second part of the book, dealing with disintegration, will be the most interesting for medical readers; it is, however, intimately bound up with the principles enunciated in the earlier pages on integration. The disorders of the nervous system are considered first as morphological, then as secretory or humoral; under the latter heading the psychoneuroses and psychoses are discussed and their morphological basis considered to be the ecto-mesodermic barrier, i.e., essentially the choroid plexus and the ependyma. To this, put forward only as a fertile hypothesis, and to related matters such as the circulation of the cerebrospinal fluid, the last seventy pages of the book are given up. In an earlier section aphasia, apraxia and agnosia are dealt with and the views of Hughlings Jackson and Henry Head appraised.

To those who would view neurology and psychiatry widely and seek biological foundations for their studies the book will be stimulating and provocative, if not provoking.

Lewandowsky's Handbuch der Neurologie: Ergänzungsband, 2te Teil, 1te Abschnitt. Spezielle Anatomie und Physiologie der peripheren Nerven. Von O. FOERSTER. S. 190 1928. Berlin: J. Springer. Price M. 38.

Professor Foerster furnishes us with a monograph that will be indispensable to every one who has to study and treat injuries of the peripheral nerves. The course, distribution and structure of the nerves have been hitherto described mainly by anatomists who are not familiar with the problems that face the clinician, but Foerster is a clinician who has investigated these problems with a purely practical end in view.

In the first section he deals with abnormal motor innervation of muscles and the anastomoses of motor nerves, and explains the variability of the palsies caused by nerve injuries. The distribution of the sensory nerves to the skin, bones and joints are similarly dealt with, and the author then describes the variations in the origin, anatomical course and branching of each nerve. Stoffel's theory, that every nerve consists of a series of isolated fascicles each of which carries fibres for the innervation of one muscle or the fibres of a sensory branch, has been accepted to explain many dissociated palsies, and certain surgical operations have been based on it; Foerster has re-investigated the matter and has again disproved the observations on which it is based. The last chapter is devoted to the anatomy and physiology of the brachial and lumbar plexuses and the muscular contractions obtained by electrical stimulation of the separate spinal roots. The volume is supplied with a large number of illustrations, many in colour, which are admirably reproduced.

Encéphalite épidémique, ses origines: les 64 premières observations connues. Par R. CRUCHET. Pp. 135. Paris: Doin et Cie. 1928. Price 15 frs.

It is generally accepted that von Economo was the first, in the spring of 1917, to recognize the clinical entity of epidemic encephalitis, but on the strength of a note published by Cruchet a month or so earlier, on certain forms of encephalitis observed on the French front, Professor Acharl proposes, in his introduction to this book, that the disease should be known as "la maladie de Cruchet," an eponymous title which the author accepts as no other title suggested for it seems to him free from objection. He publishes his records of these cases here, and in some instances gives the after-histories of the patients. Seven cases were observed in the end of 1915 and the beginning of 1916, at Commercy and Verdun, the majority of them had had syphilis, and few are recognizable examples of encephalitis lethargica. The remaining cases were seen at Bar-le-Duc, in 1916 and 1917; they are arranged in separate groups, as mental, convulsive, hemiplegic, spinal, and polyneurotic types. It is possible that a proportion of these belonged to epidemic encephalitis, but the evidence presented here certainly justifies no change in the name of the disease.

Die epidemische Encephalitis. Von F. Stern. 2te Aufl. S. 541. Berlin: J. Springer. 1928. Price M. 56.

The second edition of this monograph supplies one of the most comprehensive and complete summaries of our clinical experience of this disease which has ravaged the world during the past ten years. It is particularly the first half of the book, which deals with its clinical manifestations in both the acute and chronic stages, that will prove of most value; here all the symptoms that may appear are accurately described and, where necessary, carefully analysed. The section on the mental disturbances that occur during, and which follow, the acute illness, is especially worthy of notice. The pathological lesions of both recent and chronic encephalitis are also fully dealt with. The section on the epidemiology of the disease might have been extended with profit, but that on its aetiology and pathogenesis is admirably written; among interesting conclusions contained in it are that the virus of encephalitis is essentially different from that of influenza, and that there is only a very indirect relation between infection by these two conditions. He suggests that the later symptoms result from the action of a virus the virulence of which is augmented by general metabolic disturbances, especially due to affection of the liver.

In the treatment of the acute stages the author employs the intramuscular injection of the serum of convalescents, and cites remarkable figures in support of the claims he makes for this method: the initial mortality is reduced and the development of later symptoms is enormously diminished. Seventy per cent. of his patients so treated were fit for work three years after infection.

The best results are obtained when this treatment can be carried out in the acute stage, but it is often useful several months after the onset. Unfortunately, no equally promising therapy of the later stages can be offered.

Degeneration and Regeneration of the Nervous System. By S RAMON Y CAJAL, M.D., F.R.S. Translated by Raoul M. May, Oxford University Press. 2 volumes, pp. 769, with 317 illustrations. London: Humphrey Milford. 1928. Price £2 10s.

When Ramon y Cajal was given the Nobel Prize a number of medical men in the Argentine Republic raised a fund to publish a book by him. For the subject of this book he chose his studies on degeneration and regeneration of the nervous system, and by the aid of considerable re-investigation and data culled from his students and other scientists, he wrote in 1913 "an extensive monograph, original in large part." This Spanish book has now been translated into English, after being carefully revised and supplemented by the author. Although it is therefore in some respects not quite up to date, this fact scarcely detracts from its great value. It may be said at once that it is based almost entirely on the experimental study of lesions of the nervous system by means of the silver impregnation methods which Cajal has devised. In so far it is one sided. Changes in the myelin, in the Nissl granules and in the neuroglia are scantily treated in comparison with the changes in the neurofibrils of the cell body and of its expansions, and in the sheath of Schwann. But the changes in these structures are sufficiently complex, and they are described with the painstaking particularity which is so characteristic of Cajal's work.

The first volume of 396 pages deals with the peripheral nerves; the second of 364 pages with the central nervous system, the sensory and sympathetic ganglia and the retina. It is perhaps in this second part that neurologists will be most apt to meet with unfamiliar material. Although it was completed before the war, much that the war taught us of the histological changes following lesions of the brain and spinal cord is already fully described, as well as many other facts that could only have been observed in experimental material. The whole work is, indeed, full of data of which the most expert need not be ashamed to confess his ignorance. Except for one chapter, in which the author presents his theory of neurotropism, it is singularly free from theory.

The book is beautifully illustrated by the author's drawings, which depict clearly and completely almost every structure described. The translator has succeeded fairly well in giving the English equivalents for the new terms which Cajal has invented to describe his observations, and in making the book readable in spite of its abundant references to literature and meticulous detail of description. Full indices of the subjects and of the authors referred to in the text increase the value of the book as a work of reference.

Neurobiotaxis and other Subjects. By C. U. ARIËNS KAPPERS. Pp. 76. Copenhagen: Levin and Munksgaard. London: W. Heinemann. 1928. Price 7s. 6d.

This volume contains three lectures delivered by Kappers at the University of Copenhagen. In the first of these he recapitulates the numerous observations on which he propounded the theory of neurobiotaxis, according to which simultaneously associated impressions determine the structural connections of those parts of the nervous system that receive the impressions. He shows how this hypothesis can explain the partial decussation of the optic fibres in animals with frontally placed eyes, the arrangement of the motor and sensory representations in the cortex, and other features in the anatomy of the nervous system that have been hitherto obscure. He also brings the law of mental association into relation with neurobiotaxis.

The second lecture on the phylogenetic and ontogenetic development of the corpus striatum will be of particular interest to the physician who has not the opportunity of studying personally this important but difficult matter. He shows, for instance, that the substantia nigra develops from cells that lie in the descending strio-hypothalamic tract which springs from the palæo-striatum, and that this as well as the corpus subthalamicum consequently belongs to the striatum.

The third lecture deals with the phylogenetic development of the cortex and the functions of its different layers.

A Classification of Neurological, Psychiatric and Endocrinological Disorders. Prepared under the direction of the Committee on Classification of the American Neurological Association. New York: American Neurological Association. 1928.

No one who has devoted serious thought to the subject can deny that the present nomenclature of nervous disorders is far from perfect. This publication is a commendable attempt "to introduce some sort of order into the groupings of neurological complaints, to establish a uniform, recognized terminology and to formulate a definite scheme for classification which will not be overlapping, inclusive or antagonistic." The Committee makes a preliminary division of ætiological order into developmental defects, infection, injury, intoxication, degeneration and sclerosis, neoplasm, psycho-neurosis, psychosis, obscure, vegetative and undetermined. Within each of these foregoing categories there is an anatomical subdivision. The syndromes of cerebral arteriosclerosis are dealt with separately under the group "Vascular System." A preliminary index of common disease-terms facilitates the search for the correct grouping for each particular morbid state. By thus building up a logical classification along ætiological and structural lines, the Committee deserves praise for a laudable effort at introducing order into a state of chaos. Naturally, there are drawbacks to a scheme of this sort. In the first place a

certain amount of overlap or cross-index seems inevitable. Thus, spina bifida with meningocele will be entered into two categories; osteomyelitis of the spine might be recorded as vertebral infection, abscess of the spinal cord compression paraplegia and so on. All the varieties of tetany are relegated to the cadre of parathyroid disease, although this involves a purely speculative conception of pathogenesis which in our present knowledge seems scarcely justifiable. Again, one may question the wisdom of a deliberate exclusion of nosological terms of purely symptomatic order; in an effort to be precise there is a danger of inaccuracy. Terms such as hemiplegia, chorea, Jacksonian epilepsy—though admittedly non-committal—are for that very reason of the utmost value. A given case may be characterized by some outstanding feature the precise ætiology of which remains unrevealed; for this reason one is loath to abandon such time-honoured phraseology. Especially is this true when the exact nature is so doubtful that one is forced to record the diagnosis in the form of an alternative—for example: (?) chorea, (?) tic. Schemata of a combined ætiological and anatomical type find difficulty in accommodating disorders of obscure or unknown pathology, and special miscellaneous groupings will be required. It seems that we are not yet in a position to draw up a nosological classification which is scientifically accurate and at the same time practical. The present attempt, however, is an appreciable step in the right direction, and will assist subsequent and perhaps more adequate terminological schemata.

Modern Problems in Neurology. By S. A. KINNIER WILSON. Pp. 364.
London: E. Arnold. 1928. Price 21s.

Dr. Kinnier Wilson republishes in this volume several separate articles which have appeared from his pen in different journals during the last few years. All have been revised where necessary and some have been considerably modified, so that we have here not merely a handy collection of valuable contributions to neurology, but also the author's final and considered opinions on the problems with which they deal.

The subjects included in his twelve chapters are various forms of epilepsy, the narcolepsies, the older motor system and the new, disorders of motility and muscle tone, pathological laughter and crying, the dysæsthesiæ, and the Argyll Robertson pupil. The index provided will facilitate reference to any subject that may interest the reader.

Mongolism. By KATE BROUSSEAU; revised by H. G. BRAINERD. Pp. 210.
London: Baillière, Tindall and Cox. 1928. Price 20s.

The authors give a very complete account of mongolism, they discuss its ætiology at some length and there is a useful chapter on the differential diagnosis of the condition. The book contains some good illustrations and a full bibliography. While it does not advance our knowledge of mongolism, it will be of interest to all those who are occupied with the congenitally defective child.

Röntgenologie des Felsenbeines und des bitemporalen Schädelbildes.

Von H. W. STENVERS. S. 278, mit 324 Abbildungen. Berlin

J. SPRINGER. 1928.

That the service of radiology to neurology has, apart from the aids of special methods as the introduction of air or opaque substances into the cranio-vertebral cavities, been disappointing is possibly in part due, as the author of this monograph emphasizes, to the fact that neurologists have given little personal attention to the subject but have relied mainly on the reports furnished by radiologists, few of whom are accurately acquainted with the problems involved, or have had much personal experience. Stevens here furnishes an example of what may be done by intensive study, and though few clinicians will be able to acquire his technical skill it is important to learn how radiograms should be interpreted and how far they can help in the localization of cerebral lesions. He makes no extravagant claims, though his reason for not including ventriculography is that he believes that properly taken and carefully studied radiograms make it usually unnecessary.

The larger part of the book deals with the changes produced in the sella turcica by different types of tumours arising within it and in its neighbourhood, and by hydrocephalus and growths situated elsewhere in the brain. In the latter case distension of the floor of the third ventricle is the chief factor, and consequently the changes are most obvious when a tumour lies near this ventricle. In the last hundred pages the changes visible in radiograms of the petrous bone are described, chiefly those associated with tumours of the ponto-cerebellar angle, but the author insists on the great care that must be taken in exposing and interpreting the photographs owing to the variability in the structure of this bone.

This book is undoubtedly a valuable contribution to a subject that will certainly be developed further in the future, and it is to be hoped that the author will soon publish his experiences in the interpretation of other radiographic changes in the skull.

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EDITOR.